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TECHNICAL STUDY 35

MICROBIOLOGICAL SAFETY IN U.S. AND FOREIGN LABORATORIES

SEPTEMBER 1961

U.S. ARMY CHEMICAL CORPS
BIOLOGICAL LABORATORIES
FORT DETRICK

U.S. ARMY CHEMICAL CORPS RESEARCH AND DEVELOPMENT COMMAND
U.S. ARMY BIOLOGICAL LABORATORIES
Fort Detrick, Maryland

Technical Study 35

MICROBIOLOGICAL SAFETY IN U.S. AND FOREIGN LABORATORIES

G. Briggs Phillips

Safety Division
OFFICE OF THE SAFETY DIRECTOR

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A particular expression of appreciation is due the many scientists and directors who allowed me to study in their laboratories, to pry into their safety methodology and techniques, and to photograph their buildings and equipment. Throughout this report I have observed the wishes of those directors who, understandably, would not wish their frank discussions with me to be identified as institutional policy nor to have disparaging events, photographs, or circumstances identified with that institution. When such was not the wish or when the information had appeared in the open literature, in some instances, I have taken the liberty of revealing the name of the director or the institutional name. I am, therefore, fully responsible for the selection and identification of the report material and for any incredible or false conclusions which may have been brought about by language difficulties.

Finally, I wish to express my heart-felt thanks to my office staff, Miss Esther DeGrange and Sgt. James H. Gross, who worked many months typing the manuscript and sorting and cataloging data, photographs, and illustrations.

DIGEST

This Technical Study is an account of the research activities of the author during a Secretary of the Army Research and Study Fellowship. Some of the information gathered during this study will be repeated in different sections of this report. This repetition, however, is necessary to present the results of the study clearly and logically.

A study of microbiological safety in 102 laboratories in 18 countries shows that methods used to control laboratory accidents and illnesses vary widely and that only a few laboratories are reasonably successful. Considering the various available approaches for improving safety in the handling of infectious microorganisms, there is need for critical experimental evaluation to determine under what conditions improvements are or are not desirable and the effectiveness of those changes made. Of special interest to the Department of the Army would be the ability of laboratories throughout the free world to operate safely with infectious microorganisms under non-peacetime conditions. Through continued analysis of the world-wide status of microbiological safety and through improved communications with foreign laboratories, the Biological Laboratories could gather information applicable in its safety program and make a significant contribution to the ability of other laboratories to safely carry out biological defense programs.

FOREWORD

Laboratory technology in the handling of microorganisms infectious for man has undergone revolutionary changes during the past 20 years. In the seemingly unending struggle of man to cope with infectious diseases, the laboratories serving the medical, public health, and veterinary professions occupy a key position. These laboratories perform diagnostic services, produce and test immunizing materials, carry out research leading to the development of chemotherapeutic agents, operate in the area of national defense, serve as teaching centers, and are the instrument of the epidemiologist in assessing the prevalence of disease in the population and in administering control measures. Truly, the responsibility for maintaining adequate and up-to-date laboratory services in these fields is a great one.

Furthermore, the constantly changing pattern in regard to human infectious diseases has produced parallel changes in the operation of infectious disease laboratories. Classical diseases such as smallpox, diphtheria, typhoid fever, tuberculosis, and poliomyelitis are being brought under control in many parts of the world because of improvements in the standard of living, the application of modern sanitation methods, and greater immunization. However, since it is not yet possible to say that such diseases have been eradicated, laboratories are very much involved in their detection and control, work which increases in complexity as more diagnostic tests are used and as science learns how adaptable microbes are in resisting man's attack. In addition, new disease entities, particularly virus diseases, have been discovered with alarming regularity, presenting unparalleled challenges for laboratory scientists. We now expect the eventual isolation of the etiological agent of one or more human cancers, a feat that will undoubtedly open a new era for microbiologists and result in many changes in laboratory technology. The present-day infectious disease laboratory therefore is different from the laboratory of a few years ago, and the responsibility of the laboratory director in providing the needed service or the required research is great indeed.

In relation to this report, two often-observed laboratory phenomena are of importance. First, occupational illnesses among persons in medical and other microbiological laboratories handling infectious disease agents can and do occur and result, to a varying degree, in the interruption of laboratory functions and in temporary or permanent incapacitation or even death of laboratory workers. Second, the inability to control environment adequately, or to contain microbes properly during their laboratory manipulation, can interfere with the reliability of experimental results or laboratory determinations.

All through the history of microbiology much information has been developed on ways and means of minimizing laboratory infectious risks. Many of these observations have been recorded in the literature. However, in the past, occupational illnesses in the infectious disease laboratory were often

accepted as a normal consequence of the vocation, and little research was done on the influence of the noncontrolled environment on experiment validity. It has been principally during the last two decades that serious attention has been given to the problem of improving biological safety and reducing laboratory-acquired illnesses. The tradition of personal sacrifice is gradually becoming outdated. Also, in the last several years, it has become clear that microbiological determinations will be accurate only if the environment of the microorganism is controlled to prevent concurrent culture cross-contamination or animal cross-infection. Significantly, most methods of assuring experimental accuracy through environmental control are the same methods that are required for the control of infectious hazards in the laboratory.

Facilities, equipment, and procedures used to provide personnel safety and to control the laboratory environment are varied, and their application involves a number of skills. A "whole laboratory" concept can be evolved in which importance may be attached to such varied sub-components as management, training, building construction, air ventilation and filtration, disinfectants, immunization, and the use of special equipment and techniques. The use of recent knowledge in these areas is considered in this report under the general, and somewhat inadequate, term "Microbiological Safety." As a logical result of the application of the term one may ask a number of pertinent questions. To what extent is microbiological safety needed in various types of laboratories? Which sub-components are most important? Is the application of these newer developments fully justified from the point of view of costs?

This report will not deal exclusively or fully with the above questions but will attempt to present evaluations of the following broader questions:

1. What is the over-all status of safety in microbiological laboratories in a number of countries?

2. What specific methods are used to assure adequate safety in these laboratories?

3. What is the general attitude of scientists towards the new developments in this area?

4. Can the United States Army Chemical Corps, because of its special proficiency in the laboratory safety field, make a contribution to the "arsenal of democracy" and to medical research in general by making information on microbiological safety available to others?

5. Will an increased program for the exchange of information contribute to the mission of the U.S. Army Chemical Corps and, in particular, to the mission of the Biological Laboratories?

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FIGURES

The originals of the photographs printed in this report are on file in Safety Division, Biological Laboratories, Fort Detrick, Frederick, Maryland.

TABLES

I. INTRODUCTION

A. MICROBIOLOGICAL SAFETY DEFINED

In a broad sense, attitudes and activities which create conditions favorable for occupational infections are similar to those that lead to the occurrence of industrial type accidents. The common ingredients are people, their attitude, and the manner in which they carry out their procedures and use their tools and equipment. Since "safety" is generally understood as a term relating to the prevention of loss, one could define it by reference to (a) physical and procedural elements involved in accident prevention and (b) elements having to do with the people involved, their supervision, training, attitudes, etc. In defining "microbiological safety," however, this simple dichotomy is not completely adequate, and a more detailed definition will be used which will relate directly to some of the major topics discussed in this report.

To delimit the scope of the definition, hazards in the infectious disease laboratory can be said to fall into two principal categories; (a) those that cause physical injuries, cuts, burns, abrasions, fractures, and (b) those that cause laboratory-acquired illnesses. Microbiological safety is concerned primarily with laboratory-acquired illnesses and secondly with physical injury. Approaches for controlling laboratory hazards include vaccination, use of correct techniques, use of safety equipment, and properly designed laboratories.

1. Vaccination

Vaccination of laboratory personnel is recommended when a satisfactory immunogenic preparation is available. Good immunity is conferred after vaccination against smallpox, tetanus, yellow fever, botulism, and diphtheria. Other vaccines such as those for psittacosis, Q fever, tularemia, and anthrax are being tried experimentally with varying degrees of success. But immunogenic preparations have not been as yet developed for a number of human diseases which have been known to occur in laboratory workers. Among these are dysentery, blastomycosis, brucellosis, coccidioidomycosis, glanders, histoplasmosis, infectious hepatitis, leptospiroses, Rift Valley fever, and toxoplasmosis. We generally evaluate the efficiency of vaccines for laboratory workers on the basis of their effectiveness in preventing disease in the general population. Two possible pitfalls to this line of thinking should be mentioned. The first is that the worker may be exposed in the laboratory to infectious microorganisms at a much higher dose level than would be expected from normal public exposure. Secondly, this exposure may be by a route different from that normally expected, e.g., respiratory infection with the tularemia or anthrax organism.

2. Techniques and Procedures

The following rules for laboratory safety are well known and should be observed: (a) avoid mouth pipetting of infectious or toxic fluids, (b) use only needle-locking syringes, sterilize all contaminated discarded material, (c) frequently disinfect hands and working surfaces, and (d) do not smoke, eat, or drink in the laboratory.

Other rules may be less well understood and require more explanation: (a) do not blow out the last drop from the pipette, (b) do not mix dilutions by blowing air through the pipette into the culture, (c) wear gloves when handling a syringe containing infectious fluids, and (d) use an alcohol-soaked cotton pledget when withdrawing a needle from a rubber-stoppered vaccine bottle.

Rules or procedures pointed toward the elimination of air-borne contamination are the most important and the most difficult to institute and enforce. Once the fundamental concept of how aerosols may be produced by ordinary laboratory techniques are understood, the laboratory supervisor should attempt to eliminate or to modify those steps or manipulations that are the most hazardous and to design safety into new procedures that are developed.

3. Safety Equipment

The most important piece of safety equipment in the infectious disease laboratory is the ventilated safety cabinet. The basic requirements for the cabinet are (a) sufficient inward air flow or operation at a negative pressure, (b) filtration of exhaust air, (c) a shielding glass panel between the operator and the operation, and (d) means of sterilizing both the exhaust air filter and the interior of the cabinet.

Other types of safety equipment have been developed to safely carry out certain hazardous procedures such as blending and centrifuging. Much of this safety equipment is commercially available, and source information can be made available. A partial list of safety equipment would include inoculating loop incinerators, pipetting devices, safety centrifuge cups, safety blendor bowls, and filter facial masks. The latter are mentioned because of the well-known inefficiency of the common hospital gauze mask in filtering out air-borne particles. Filter masks with high filtering efficiencies suitable for laboratory or animal room work are now available. However, since the ventilated cabinet will contain any spill or aerosol that may be generated, the cabinet is generally the first type of safety equipment that should be provided.

4. Building Facilities

Design criteria for laboratories that augment and improve safety have been developed by the U.S. Army Chemical Corps and others. As the demands upon the microbiologist increase, certain building design features

cease to be mere advantages and become necessities. Among these may be mentioned (a) building ventilation, (b) control of direction of air movement, (c) filtration of air, (d) separation of areas of different risk levels, (e) use of germicidal vapors, gases and radiations, and (f) separation and improvement of holding facilities for infected animals.

5. Management Aspects

The management approach of programming, regulating, reporting, training, and selecting, is perhaps the most important method of controlling laboratory hazards, although it is interrelated and overlaps with the other approaches mentioned. The management approach also attempts to include control of the "human factor" in the application of the other principles.

Microbiological safety may be defined, therefore, as that blend of the above listed elements which can be used in an infectious disease laboratory to reduce the risk of occupational illnesses. Obviously different laboratories, with varying functions, would require varying portions of each of the five ingredients for a satisfactory microbiological safety program.

Any program of loss-prevention is based on the dual premise that (a) the loss (in this case laboratory-acquired illness) is the result of a series of events which result in an accident and, (b) accidents are largely preventable by controlling these events. Translated to the present problem this means: (a) accidents or wrong techniques which have not been "safety tested" create conditions for infection, and (b) if the accident was preceded by any predisposing human or physical factors, these must be corrected in order to prevent recurrence.

B. OBJECTIVES OF THE STUDY FELLOWSHIP

This study of microbiological safety in U.S. and foreign laboratories was made possible by a Secretary of the Army Research and Study Fellowship awarded to me in August 1958. The specific objective of the research program was to obtain precise and detailed information on the status of microbiological safety in U.S. and foreign laboratories.

The need and justification for obtaining information on microbiological safety arises from the specific interests and activities in this field by the U.S. Army Biological Laboratories and from the increasing interest in this subject in U.S. medical research circles in general. During the past 18 years the Biological Laboratories have maintained an active research and development program on microbiological safety. This program has allowed research with highly infectious human pathogens to proceed without large-scale incapacitation of laboratory workers and has provided complete protection for the human and animal population in the surrounding community. Interest in microbiological safety and the need for development of methods to reduce laboratory-acquired illnesses have been emphasized by a number of

published reports on outbreaks of laboratory-acquired infectious diseases and by a survey published in 1951 by Sulkin and Pike.[17]* This survey summarized information on 1342 illnesses contracted in infectious disease laboratories. These reports will be discussed in detail in Chapter III.

In spite of the large amount of technical information on microbiological safety available in scattered publications, no single treatise has as yet been prepared dealing with the many facets of the problem. Judging from the frequency with which the U.S. Army Biological Laboratories have been called upon by other Government agencies, private research institutions, universities, and foreign governments to supply information and consultative service on microbiological safety problems, there is a general and increasing need for such a treatise.

An effort to summarize information on microbiological safety technology would be thwarted by lack of information in several areas. First, it is known that much information on methods for reducing laboratory infectious risks does not reach adequate distribution channels. Such safety procedures may have been developed by specific research or may have developed through trial and error. In either case there has been little incentive for scientists to publish such "how to do" information. Second, a compilation of information on microbiological safety should be a practical document aimed at real and existing needs. But little information is available on the status of the acceptance of existing safety information in U.S. and in foreign laboratories. Finally, no specific effort has been made to analyze problems, developments, and needs in foreign infectious disease laboratories.

The principal purpose of this study, therefore, was to obtain information on the status of microbiological safety which could be used for a monograph or summary of information in this field. Other objectives, however, were of more immediate importance. For example, the ability of infectious disease laboratories in any country to function on a sizeable scale using highly infectious agents without laboratory-acquired illnesses indicates that laboratory's ability to serve effectively in case of epidemics or in case of military attack with biological agents. Likewise, competence in safety technology is, in part, a measure of a laboratory's ability to carry out a research program on offensive and defensive aspects of biological warfare. Another objective was to obtain information on safety technology from various laboratories which could be of immediate and practical importance to the mission of the Biological Laboratories. Finally, information gathered on an international scale might be helpful in developing biological laboratory programs for newly-developing countries. The latter point can be underscored by citing the interest in this subject which has been expressed by The World Health Organization.[2]

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* See Literature Cited.

In summary, the objective of the Research Fellowship was to obtain detailed information on the present-day, world-wide status of microbiological safety. This information properly analyzed, would allow realistic evaluation of present and future needs and reveal avenues of endeavor that could be used to avoid human infection in the laboratory.

C. METHODS AND DETAILS OF THE STUDY

The study was conducted during the period 22 February 1959 to 15 June 1960 with official travel to selected laboratories during the period 15 April 1959 to 10 March 1960. The remaining time was spent in arranging appointments and in the preliminary preparation of reports. Studies were done in 111 laboratories in 60 cities located in 18 countries. These are tabulated in Table I. Appendix A lists the laboratories and institutions visited, including the name and the address of the head of each laboratory. Types of laboratories included in the survey were:

Schools of Medicine, Public Health, or Hygiene	47
National, State, or Municipally Owned Laboratories	27
Hospital Laboratories	14
Commercial Organizations	11
Science or Agricultural Schools	6
Defense Organizations	4
Veterinary Schools	2
TOTAL	111

In addition to the 111 laboratories, the facilities of 11 hospitals in seven countries were inspected. During the travel, approximately 20 invitations were received to visit other laboratory institutions. Because of time limitations and prior commitments, only five of the invitations were accepted.

During the Fellowship year I travelled 80,965 miles, apportioned as follows:

Air miles	57,714
Automobile miles	14,000
Boat miles	6,361
Train miles	2,890
	80,965

Before beginning the study an initial list was prepared of some 200 candidate laboratories. This list was compiled primarily from suggestions offered by laboratory scientists at the Biological Laboratories, The National Institutes of Health, The Communicable Disease Center, and several U.S. universities. The laboratories visited during the study were selected from the candidate list on the basis of probable use of infectious agents, geographic location, and willingness to allow a short study and inspection

of their methods and facilities for microbiological safety. Surprisingly, no more than about ten of the laboratory directors initially contacted failed to reply or preferred not to participate in the study. In this manner the candidate list was narrowed to some 130 laboratories in 19 countries. It was intended that at least 100 of these would be included in the final selection.

TABLE I. COUNTRIES, NUMBER OF CITIES, AND LABORATORIES VISITED DURING THE STUDY FELLOWSHIP

COUNTRY	CITIES	LABORATORIES
Australia	5	10
Austria	1	1
Canada	2	6
Denmark	1	1
England	6	18
Finland	1	4
France	1	1
Germany	10	11
Greece	1	4
Italy	1	1
Japan	1	1
Netherlands	3	3
Norway	2	6
Portugal	1	1
Scotland	3	5
Sweden	5	14
Switzerland	2	2
United States	14	22
TOTALS	60	111

Final arrangements were made by correspondence with each laboratory director at least three weeks prior to the visit. These generally included the approximate length of the visit, a general outline of the information to be discussed, and time and dates for the presentation of illustrated lectures.

The time spent at each laboratory varied from one to five days, averaging two to three days. Following each visit, time was reserved for the preparation of a trip report in which pertinent observations and details were recorded.

The techniques used to collect data or to stimulate exchange of information were as follows:

1. Discussions with single or small groups of individuals. An attempt was made during interviews to maintain an informal atmosphere. Although the questions asked at each laboratory were essentially the same, they were varied to suit the situation and presented informally rather than as a questionnaire or check list. Whenever possible I made written notes during discussions. A total of 412 scientists and laboratory technicians were interviewed.

2. Inspections of building facilities, laboratory equipment, and laboratory techniques. In general laboratory heads were quite willing or even anxious to have their building facilities and laboratory equipment inspected but less desirous of prolonged observations of the procedural techniques being used. Nonetheless, this proved to be one of the most fruitful methods of gathering information. Whenever possible I requested that I be allowed to visit in turn with the scientist in charge of each laboratory unit, rather than being taken on a guided tour by the laboratory director. In this manner a more detailed study of facilities, equipment and techniques was possible. Permission to take photographs of facilities, equipment, and techniques was given at 83 laboratories (75 per cent). During the study several thousand color slides on 35 mm Ektachrome film were taken. These proved invaluable as a means of quickly recording information and observations for later study and as an efficient means of demonstrating unusual equipment or techniques. Selected photographs from this collection are included in this report.

3. Collection of written reports, reprints of published articles and design drawings of buildings and equipment. Laboratory directors were unusually cooperative in this regard. Subsequent study of the several hundred reprints and reports proved valuable in evaluating each laboratory. In several instances I was provided with printed rules and regulations formulated for microbiological safety. Also, at two laboratories (in Sweden) detailed building construction drawings were provided which proved to be valuable source material.

4. Forty-six illustrated lectures on microbiological safety were presented to U.S. and foreign audiences. In addition to serving to encourage communication and the exchange of information, discussions and questions following most of the lectures were a good source of information.

5. Safety questionnaires were used as a possible device for collecting further data, particularly information on safety attitudes. This attempt, however, was for the most part a failure. Most laboratory directors preferred not to ask their staff and technicians to fill out the anonymous, one-page questionnaire prepared for this purpose. A total of 202 questionnaires were returned from seven countries.

Although the nature of the information collected varied because of the different types of laboratories involved, local conditions and customs, and other factors, at each laboratory an attempt was made to secure information under the following headings.

1. Type of laboratory work done, infectious agents used, and approximate amounts handled
2. Existence of a formal or informal safety program
3. Reporting procedures and accident analysis methods
4. Regulations for microbiological safety
5. Attitudes and concepts of social responsibility for occupational illnesses
6. Relationships between professional and nonprofessional workers
7. Procedural methods used or not used to reduce infectious hazards
8. Presence or absence of safety equipment
9. Frequency of occupational illnesses and deaths
10. Building facilities and laboratory design criteria
11. Methods of decontamination or sterilization of air, fluids, and solids
12. Methods of handling animals
13. Use of germicidal gases or radiations
14. Precautions used in aerobiological experiments
15. Limitations imposed because of inability to control microbiological hazards
16. Future plans for new buildings, etc.
17. Present needs in terms of information, equipment, money, etc.

Of the 111 laboratories studied, nine were eliminated in most of the final tabulations either because of little use of infectious agents or because of inadequate information for proper analysis. Data from the 102 laboratories acceptable for analysis were studied individually and then grouped under selected sub-topics. In most cases it has been necessary to preserve the anonymity of specific laboratories according to the wishes of the laboratory directors.

In presenting such a large quantity of both subjective and objective data, it is difficult to achieve the desirable degree of brevity. However, the chapter arrangements provide a logical division of subject matter. Most chapters are begun with a summary.

II. LABORATORY-ACQUIRED INFECTIONS

A. SUMMARY

Since the study fellowship was concerned with ways and means of preventing occupational illnesses among laboratory workers, it is helpful to present, in this early chapter, a summary of existing knowledge on this subject. By referring to laboratory-acquired illnesses of scientists, to specific outbreaks of disease in laboratories, and by summarizing the results of laboratory infection surveys, the significance of the problem is indicated. Next, by presenting information on laboratory illnesses collected during the study fellowship, a general comparison can be made with former data. Finally, general information on the acts or accidents known to have caused laboratory-illnesses is examined. Here, past information can be compared with data collected during the study fellowship.

The data presented in this chapter leave little doubt that in most infectious disease laboratories infection of workers has been and still is a problem of considerable concern. Statistics collected during the study are not markedly different from that of other surveys. The death rate for laboratory illnesses is three to four per cent. All data available, including the present research results, indicate that approximately 80 per cent of laboratory occupational illnesses are not the result of overt accidents and therefore are probably due to aerogenic contamination of the laboratory environment by "normal" manipulations of infectious materials. Among the 20 per cent of the illnesses which followed known accidents, the most frequent single cause was accidental self inoculation with a syringe and needle.

B. PAST INFORMATION ON LABORATORY INFECTIONS

Opinions concerning laboratory-acquired illnesses vary. The idea that such illnesses are normal occupational hazards, however, has been for the most part discarded. The concept of allowing apparent or inapparent illnesses to occur in order to gain resistance has been supported with some diseases, but this is open to criticism and not applicable to all infectious agents. In the final analysis and in the interest of efficient management and humanitarianism, the aim of all persons handling disease producing agents should be to acquire the knowledge, techniques, and equipment to enable them to work without becoming infected.

Collection of biometric data concerning the frequency of laboratory-acquired infections is complicated by factors such as: (a) nondiagnosed apparent or inapparent diseases, (b) reluctance of many laboratories to report occupational illnesses, and (c) absence of formal and systematic channels for reporting infections. It is probable, therefore, that instances of laboratory-acquired disease reported in the medical and other literature represent only a fraction of those actually occurring.

The laboratory infection may be mild in nature and may even be unrecognized, but all too often serious economic and physical consequences result. Although the means by which the illness is acquired is sometimes unknown, aerosols created by accidents and poor techniques are common causes.

Of utmost importance in the epidemiology of laboratory infections is the fact that, in the laboratory, there are frequent exceptions to the natural mode of infection. Tularemia and anthrax in nature are rarely found as respiratory infections but among laboratory workers could easily be confused with other common respiratory ailments. The importance is further emphasized by the fact that respiratory anthrax is rapidly fatal, and the diagnosticians' verdict is generally given posthumously.

Newly isolated and discovered disease agents often infect the laboratory personnel who handle them. Indeed, one highly lethal viral agent, monkey B-virus, Herpesvirus simiae, has never been noted in humans except in laboratory people and others working in and around monkeys. Since the first case in 1932, there have been 15 cases with 13 deaths.

Louping ill, an encephalitic disease of sheep in Scotland, was discovered in 1930, yet six laboratory workers were infected with the causative virus before the first case outside of the laboratory was recognized. Six infections with the rickettsia of Q fever from laboratory sources were diagnosed, beginning in 1938, before the disease was discovered among workers in meat packing factories. A more recent example is the disease called rickettsialpox, caused by Rickettsia akari. Shortly after its discovery in New York City in 1946 there were four laboratory-acquired cases of the disease. Coxsackie virus, discovered in 1948, has infected a number of laboratory workers, as has the ECHO and other new viral agents.

Some of the well known parasites which have caused fatal laboratory infections are: Brucella melitensis, Shigella dysenteriae, Pasteurella tularensis, Salmonella typhosa, poliomyelitis virus, yellow fever virus and Rickettsia rickettsii.

In 1886 a Peruvian medical student by the name of Carrion inoculated himself with the blood of a patient suffering from verrugas. Carrion died of Oroya fever thus showing that the two diseases were caused by the same organisms. In the early 1900's Lazear, a member of the Walter Reed Commission, died of yellow fever after having been accidentally bitten by a mosquito. Scientists studying disease transmission in Africa died of the same disease more than 25 years later. Ricketts died in Mexico in 1910 from typhus fever, a disease whose causative organism was named for him. A. W. Bacot, who had done much work with plague, yellow fever, and trench fever, died in 1922 of typhus while studying the infectivity of louse excreta. Otto Obermeier, the well-known discoverer of the organism causing relapsing fever, died at the age of 30 of cholera contracted in the laboratory. Professor Conti, a highly respected investigator of psittacosis died on 7 January 1936 from a laboratory infection with that virus. At the age of 48, in July 1936, Dr. Breinl, the Director of the Hygiene Institute of

The German University, died of an infection with Brazilian spotted fever. No doubt a long list of outstanding medical scientists who have died or have been severely handicapped as a consequence of laboratory-acquired infections could be compiled.

The Germans were perhaps the first to publish collected cases of laboratory illnesses. A summary of 59 laboratory-incurred cases of typhoid fever occurring in that country between the years 1915 and 1928 was published in 1929 by Kisskalt.[3] There were five fatalities. Of these, twenty-one cases, or 36 per cent, were thought to have been caused by sucking infectious fluids into the mouth. Other probable causes for the infections were: spilling or spraying cultures, 4 or 7 per cent; using contaminated pipettes, 3 or 5 per cent; eating in the laboratory, 3 or 5 per cent; washing contaminated glassware, 1 or 2 per cent; smoking in the laboratory, 1 or 2 per cent; and preparing vaccines, 1 or 2 per cent. Causes for the remaining cases were not known.

Kisskalt also reviewed 24 laboratory infections, with three deaths, caused by other bacterial pathogens. One nonfatal diphtheria infection was said to have been caused by aerosols that escaped from a hood in which respiratory challenge experiments were being conducted.

In the late 1930's, Draese published the results of an investigation of 111 laboratory infections, with nine fatalities, occurring in Germany during 1930 to 1937.[4] He also mentioned 157 infections, other than typhoid, which had been reported in the German and other literature. Draese also mentioned 130 cases of laboratory infections with typhoid previously reported by Kisskalt in 1915 and in 1929. During 1925 to 1936 there were 39 cases of laboratory-acquired typhoid fever among workers of the German Public Health Service. In his publication Draese declined, because of their high frequency, to list laboratory infections of Weil's disease (infectious jaundice) and yellow fever. One case reviewed by Draese involved the simultaneous infection of a laboratory worker with two strains of dysentery and one strain of paratyphoid.

A number of U.S. publications in the last 30 years have described laboratory outbreaks of specific diseases. The diseases described most frequently are brucellosis, psittacosis, coccidioidomycosis, and Q fever.

A summary of 74 brucellosis infections occurring in a number of laboratories was published in 1941 by Meyer and Eddie.[5] Huddleson and Munger,[6] in 1940, published details of an epidemic of brucellosis at Michigan State College. Between December 10, 1938 and February 10, 1939 forty-five clinical cases occurred among personnel associated with the bacteriological laboratories. In addition there were 40 possible subclinical infections. The infecting organism was Brucella melitensis, cultures of which had been centrifuged several times in an enclosed Sharples centrifuge in the hallway of the basement of the laboratory building. Forty-one of the 45 clinical cases occurred in college students. One laboratory stockroom attendant,

one plumber, one stenographer, and one salesman were also infected. Although the original publication indicated no infection source which could definitely have been responsible for the infections, the possibilities eliminated by the investigations left little else but that of air-borne contamination and spread of brucella organisms throughout the building. Only one of the students had ever been in the brucellosis laboratory located in the basement. The students were not allowed to handle brucella cultures or infected animals, and the student laboratories were on other floors of the building. Other infected individuals had no direct contact with the brucella laboratory. In the light of recent knowledge on the hazards of centrifuging it is highly probable that the basement-located centrifuge created aerogenic contamination with spread through the entire building.

Among the several outbreaks of disease which have occurred in laboratories of the National Institutes of Health was the infection with psittacosis of 11 of 54 employees of the Hygienic Laboratory building in Washington, D.C. The report by McCoy in 1930[7] showed that only three of the 11 infected individuals had had direct contact with psittacosis cultures or infected birds. None of the remaining eight persons were allowed in the psittacosis laboratory. Consequently it was felt that the infections resulted from aerogenic spread of the virus.

Sulkin and Pike[1] have stated that "Coccidioides outnumbers all other fungi as a cause of laboratory infection, due undoubtedly to the highly infective nature of the chalamydospores." A number of laboratory infections have been reported in the literature.[8-11] Dr. C. E. Smith of Stanford reviewed in 1950 those cases occurring in his laboratory between 1929 and 1949 and other cases which had not been previously reported.[12] At Stanford there were 36 proved, 15 probable and nine possible laboratory infections with Coccidioides immitis. Twenty-nine of 51 proved or probable cases were among persons who worked in other laboratories in the building or who had been merely visitors. Only three of the infections followed a definite and known accident. In addition to these infections, Smith reported ten confirmed and two probable laboratory-acquired infections which had occurred in other institutions. He concluded that a grave risk exists when growing this fungi on solid media. The mode of transmission is aerogenic, and, when allowed to escape, the chalamydospores can easily infect laboratory personnel, others throughout the building, and even visitors.

At least four significant laboratory outbreaks of Q fever have been reported in the literature since 1940. In that year, during a 54-day period, 15 of 153 persons working in one laboratory building of the old National Institutes of Health developed roentgenological, clinical, and serological evidence of Q fever pneumonitis.[13] Work with Q fever rickettsia was confined to a laboratory on the second floor. The distribution of the cases according to the main work place of the building employees was as follows:

Floor Assignment	Number of Employees	Number of Infections
Basement	34	4
1st floor	39	0
2nd floor	41	4
3rd floor	39	7

Aerogenic spread of the infecting agent was the best means of explaining this outbreak.

In 1946 an outbreak of Q fever occurred among the personnel of the 15th U.S. Medical General Laboratory in Italy.[14] As a result of the detection of the disease in American and British troops in that country, infected guinea pigs had been sent to the general laboratory for investigation. In a three-month period following receipt of the animals there were 20 cases of Q fever among the laboratory personnel or visitors to the laboratory. It was concluded that "the most likely mode of transmission was by inhalation of the infectious agent which became suspended in the air of the laboratory in spite of reasonable precautions."

In the same year at Fort Bragg, North Carolina, there were 16 cases of Q fever among personnel of the laboratories of the Commission on Acute Respiratory Diseases.[15] Infected personnel worked in several different rooms of a laboratory building. The spread of the infecting agent, again by air-borne means, was felt to be connected with the processing and harvesting of infected eggs.

The largest reported laboratory outbreak of Q fever occurred in a single building of the National Institutes of Health between December 1945 and May 1946.[16] A total of 47 persons, including persons who had merely visited the building for a short time, became infected. No infections occurred in persons working in the Q fever laboratory on the first floor. Almost all had either previously been infected or were immune. Cases were widespread throughout the remainder of the building as indicated below:

Floor Assignment	No. of Workers	No. of Cases	Percentage Infected
Basement	18	8	44.4
1st floor	27	16	59.3
2nd floor	6	2	33.3
3rd floor	11	4	36.3
Attic	5	1	20.0
Circulating	15	5	33.3
TOTALS	86	36	43.9

A relationship was noted between the appearance of laboratory cases and times of peak production of live Q fever antigen. This operation involved the centrifugation and resuspension of yolk sac material. There can be no doubt that air-borne processes were involved in this outbreak. In addition to the human cases detected, 20 guinea pigs in the building, 15 on the

first floor and 5 in the attic, were found to show strongly positive Q fever serological reactions, whereas earlier tests had been negative.

Taken together the above instances of laboratory outbreaks of disease demonstrate how air-borne infectious agents can be spread throughout an entire building, incapacitating not only persons directly handling infectious materials but others in the building including visitors. Although such outbreaks may be rare they are a potential in any infectious disease laboratory that might be called upon to handle new or highly infectious, disease producing materials. Tables II and III summarize, as illustrative data, laboratory infections occurring in the U.S. Public Health Service between 1910 and 1950 and four specific outbreaks of laboratory infections.

TABLE II. SUMMARY OF ALL U.S. PUBLIC HEALTH SERVICE LABORATORY INFECTIONS 1910 TO 1950

DISEASE	TOTAL NUMBER OF CASES
Q Fever	78
Typhus	47
Tularemia	33
Spotted Fever	28
Psittacosis	11
Brucellosis	10
Others	24
TOTAL	231

TABLE III. SPECIFIC OUTBREAKS OF LABORATORY INFECTIONS IN THE U.S. PUBLIC HEALTH SERVICE

DISEASE	INFECTIONS AMONG			TOTAL INFECTIONS	TOTAL BUILDING EMPLOYEES	YEAR
	Workers in Rooms Where the Disease Studied	Employees from Other Areas in Building	Delivery Men, Visitors			
Psittacosis	2	8	1	11	57	1930
Q Fever	0	15	0	15	153	1940
Q Fever	0	47	3	47	142	1945-6
Typhus	6	7	0	13	?	1942-3

A number of publications have been concerned specifically with the incidence of tuberculosis among medical and laboratory personnel.

Hedvall[17] studied tuberculosis morbidity among medical students at Lund University in Sweden during the years 1930 to 1937. The occurrence of active tuberculosis in medical students was compared to students majoring in philosophy, theology, and law who lived under similar conditions. The results are shown in Table IV. It was felt that in 16 of 47 cases of primary infection among medical students there was a significant connection between the course in general pathology and the time of skin test conversion. Hedvall stated that the medical students themselves had long suspected that the course constituted a source of tuberculosis infection. In spite of the precautions regarding cleanliness during autopsies, tubercle bacilli could be recovered from the rooms and from various objects in the rooms (towels, trays, dust from autopsy tables) by culture and by guinea pig inoculation for as long as 24 hours after autopsy of a tuberculous subject. During a two-year period Hedvall was apparently able to eliminate conversion of tuberculin negative students during the pathology course by introducing more stringent precautions and decontamination procedures and by limiting necropsy of tuberculous patients by students.

TABLE IV. INCIDENCE OF TUBERCULOSIS AMONG SEVERAL STUDENT GROUPS AT LUND UNIVERSITY, 1930 TO 1937 (After Hedvall)

STUDENT GROUP	NUMBER OF PERSONS EXAMINED	NUMBER OF TB CASES FOUND	PER CENT TB
Medical	638	72	11.3
Philosophy	1,367	17	1.2
Theology	409	12	2.9
Law	488	9	1.8
Probationary nurses	434	23	5.3
TOTAL	3,336	133	

Morris[18] reported the results of a 12-year tuberculosis control program in a women's medical college. During this time there were 56 active cases of tuberculosis among 449 female medical students (clinical morbidity rate of 12.5 per cent). There were six deaths; a mortality rate of 1.3 per cent and a case fatality rate of 10.7 per cent. The primary infection rate was 100 per cent. In the active cases, Morris estimated the total time spent in recuperation by the group with active infections to be more than 100 years. She believed that the autopsy service and the use of actively infected patients for demonstrations in physical diagnosis and clinical training constituted the primary sources of infection in routine medical school procedures.

Lim-Yuen[19] investigated the incidence of primary tuberculosis among 559 staff members of a sanitorium in Canada during a six-year period. The tuberculin conversion rate was 37.4 per cent per annum. Members of the staff in closest contact with tuberculosis patients accounted for 98.7 per cent of the conversions. During this period, there were 12 cases of active tuberculosis, eight among ward attendants but none in the nursing staff. Lim-Yuen believed that the exposure potential of ward attendants and nurses was about the same but that the discipline and training of the latter was a large factor in ensuring their safety. Staff members who were originally negative tuberculin reactors had a morbidity incidence of 3.8 per cent per annum, while that of the positive reactors was 0.89 per cent per annum.

G. S. Smith[20] in 1953 reported conclusions resulting from a questionnaire mailed to all members of Association of Clinical Pathologists in England. Answers were received from 102 departments where approximately 192,000 necropsies had been performed. Of these, approximately 9000 were active tuberculosis cases. On the basis of the number of infections occurring among personnel (two doctors and eight technicians) Smith concluded that the necropsy room was not a serious source of tuberculosis infection to hospital staff personnel. Medical students were not included in this survey. Smith stated that several correspondents expressed the view that the laboratory was a greater potential source of infection than the necropsy room.

Meade[21] studied tuberculin skin test conversions in a medical and dentistry school. Preliminary studies indicated that the highest number of conversions occurred during the second school year, the year during which courses in pathology were taught. Tuberculosis autopsies for second year students were eliminated and skin test information gathered over a period of about three years was compared with a former equivalent period during which students handled tuberculous material. The results were as follows:

	No. of TB Autopsies	No. of TB Conversions	Total No. Students	Per Cent Conversions During 2nd Year
Period during which TB autopsies performed (6 classes)	81	112	139	80.5
Period during which no TB autopsies performed (4 classes)	0	6	156	4.0

These data appear to be overwhelming evidence of the effect of handling tuberculosis materials on primary tuberculosis infections. Meade's description of the technique used in the pathology course is of interest and is quoted in part below.

"During the course the classes of 40 to 60 students were divided into groups of four who were on call in rotation to participate in all autopsies. Students donned gown, apron and gloves, but did not wear masks and they actively assisted a department member in performing the autopsy. The student assistants helped to remove, open, section, clean, and examine all the organs. They were instructed on how to remove contaminated gloves and aprons but were not supervised after the initial instructions. In addition to assisting in autopsy performance, all students were given the opportunity once each week to handle and examine all tissues from the autopsies of the previous week, including those on tuberculous subjects. This material was unembalmed, refrigerated, and displayed in open pans about the autopsy room, and students were encouraged to feel and examine the specimens closely. Thus, there was an opportunity for all students to have close contact with all the tuberculous material from autopsies performed during the course in pathology."

"During the years covered by the study there were, on the average, 13 to 14 autopsies performed each year during the pathology course on tuberculous subjects with which students had opportunity for contact in the manner described."

Reid,[22/] in 1957, reported the results of a survey on the incidence of tuberculosis in medical laboratory personnel in the United Kingdom. Preliminary observations, made by comparing "claim" rates reported to the Ministry of Health, indicated the frequency with which various medical workers acquired active tuberculosis during the period 1953 to 1955.

	Number of Cases	Man Years Exposure	Rate Per 1000 Per Annum
Pathologists	12	2,193	5.47
Chest Physicians and Surgeons	10	2,489	4.02
Other Medical Staff	13	19,830	0.66
Laboratory Technicians	33	11,593	2.85
Other Auxiliary Staff	34	32,152	1.06

The above data represent a total of 102 active cases acquired by hospital employees during the designated period.

A survey was made of 368 medical laboratories in England. Information on type of laboratory, laboratory conditions, nature of hazards, X rays and tuberculin skin testing, number of persons at risk and number of cases of tuberculosis was obtained for the five-year period, 1949 through 1953. The number of persons working in the 345 laboratories replying to the questionnaire was 4828. Although 151 cases of tuberculosis were reported, only 96 pulmonary cases were accepted for the analysis. Age-sex-specific notification rates for the United Kingdom during these years were used as a basis of comparison. Figures 1 and 2 are taken from data presented by Reid.

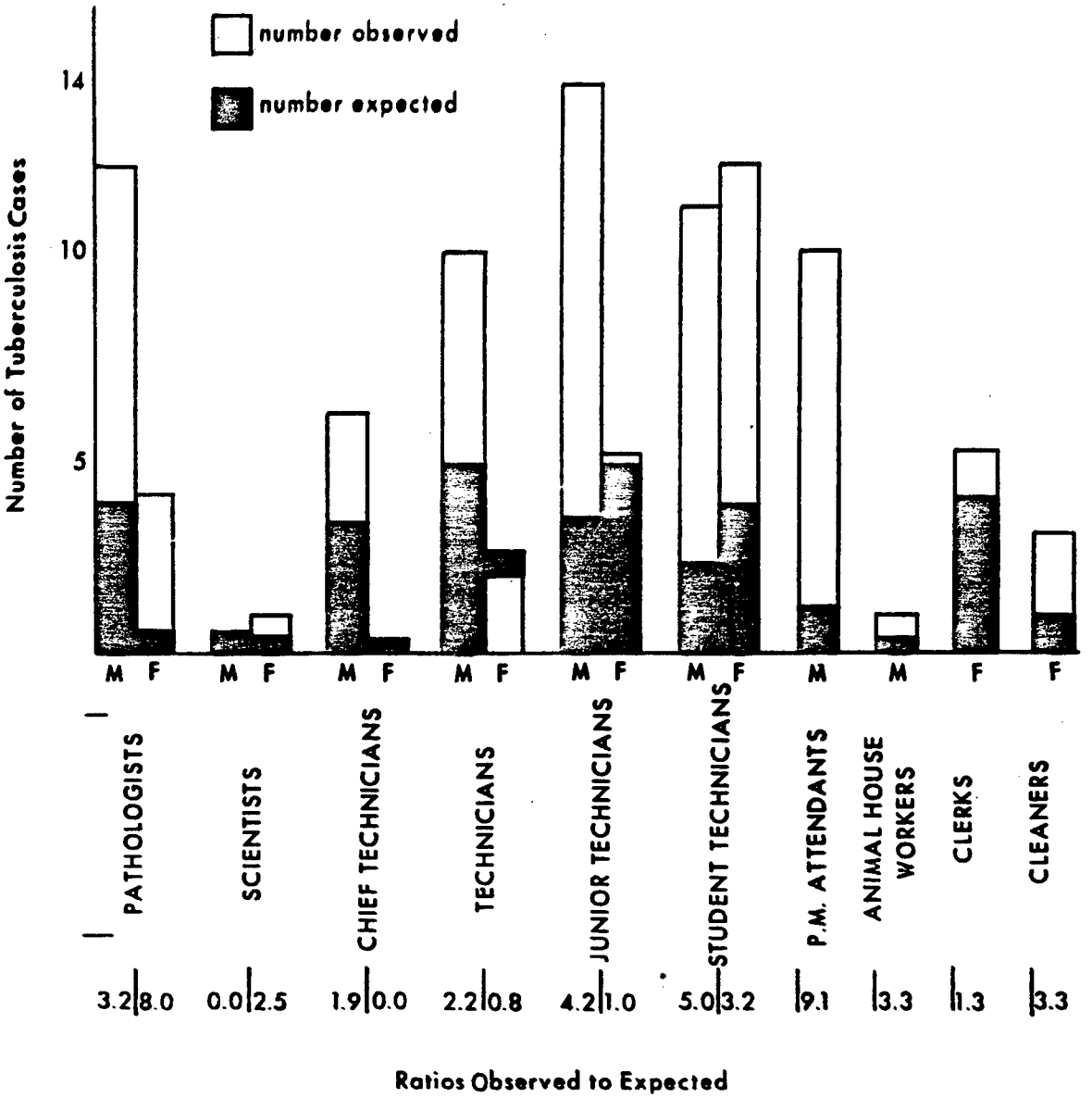

Figure 1. Comparison of Observed Frequency of TB in Medical Laboratories in the United Kingdom with the Numbers Expected from National Notification Rates, 1949 to 1953. (After Reid)

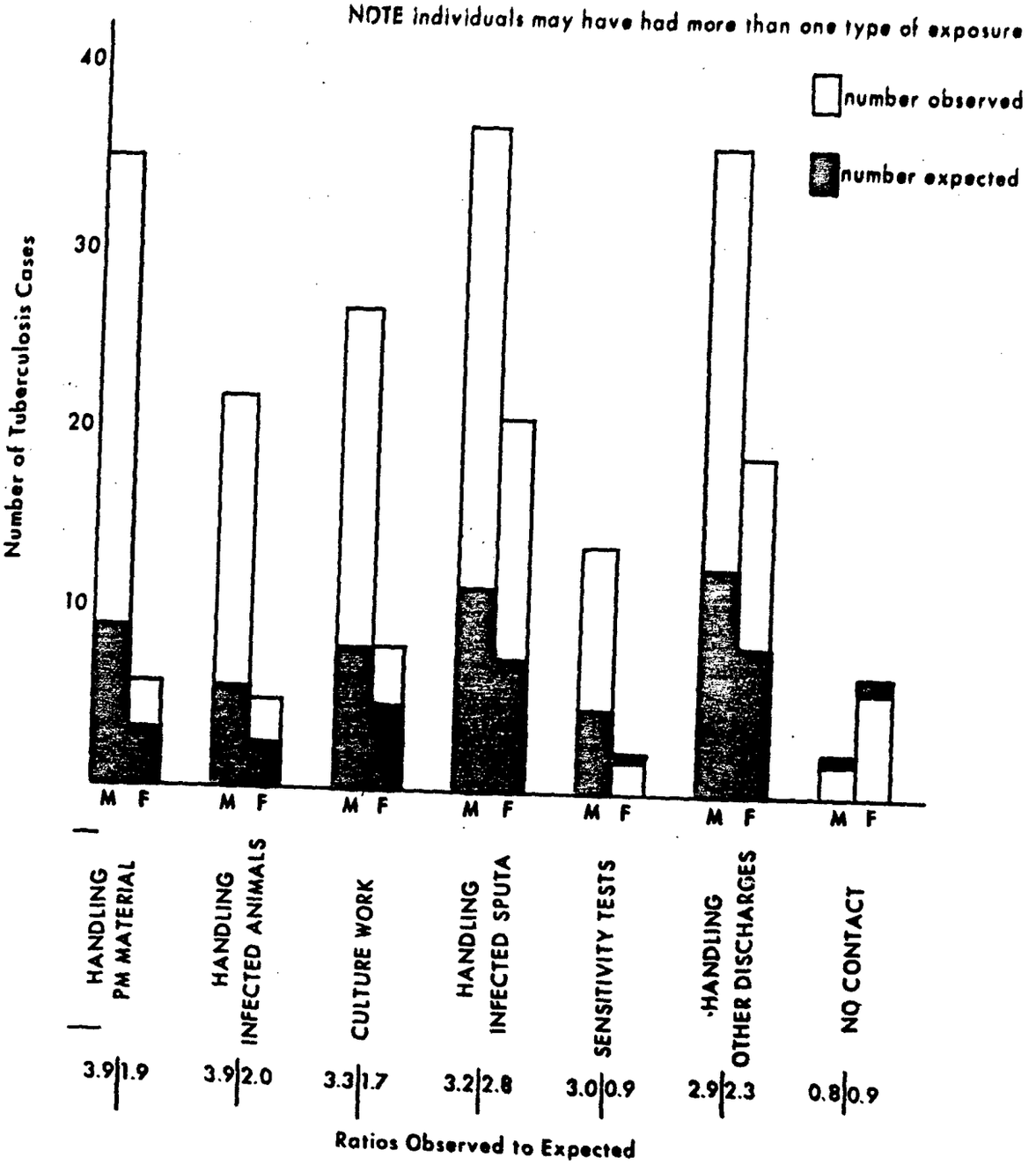

Figure 2. Cases of TB in Medical Laboratories in the United Kingdom According to Contact History Compared with Numbers Expected at National Notification Rates, 1949 to 1953. (After Reid)

Male pathologists, junior and student technicians, post-mortem attendants, female pathologists, student technicians, and cleaners appeared to contract pulmonary tuberculosis more frequently than would be expected from the comparison rates. The risk for males of various work categories, in decreasing order, was apparently (a) handling of post-mortem material and infected animals, (b) culture work, (c) handling infected sputum, (d) sensitivity tests, and (e) handling other discharges. There was some indication that the incidence of tuberculosis was at a peak among persons who had been employed for about two years.

To test his analysis method Reid compared the ratios of observed to expected cases in three categories of hospital workers with the observed vs expected incidence of tuberculosis among non-hospital, civil employees who he considered to have roughly comparable educational and social backgrounds. The ratios determined by Reid are as follows:

Occupation	Ratio of Observed to Expected Incidence of Pulmonary Tuberculosis
Male Pathologists	3.2
General Post Office Professionals	0.7
Male Laboratory Technicians	3.1
Male Post Office Clerks	0.9
Female Laboratory Technicians	1.7
Female Post Office Clerks	0.9

Reid concluded that the incidence of pulmonary tuberculosis severe enough to cause loss of work time was about three times as high among laboratory personnel exposed to infected materials as among nonexposed laboratory personnel. Pathologists and laboratory technicians have a much higher incidence of tuberculosis than do socially comparable groups.

Reid stated, "Strong though such circumstantial evidence is, it simply indicates that a hazard exists without determining whether air-borne dissemination or contact contamination is the only or even the more important mode of transfer of infection. There is thus a clear need for detailed bacteriological studies of technical procedures as a source of infection. In this way, more specific prophylactic measures can be added to more obvious hygienic precautions."

In Canada, Merger,[23] in an effort sponsored by the Laboratory Safety Committee of the Canadian Society of Laboratory Technologists, collected data on tuberculosis infections among technicians working in the Departments of Health in each Province. A total of 42 cases were listed from eight Provinces during the years 1943 to 1955. Of these 38 per cent occurred in Ontario during the years 1952 to 1954. After estimating the number of exposed laboratory technicians, Merger calculated the annual

laboratory infection morbidity rates during certain years and compared them with morbidity figures for the general population. These data are summarized in Table V.

TABLE V. A COMPARISON OF TUBERCULOSIS MORBIDITY RATES AMONG LABORATORY TECHNICIANS AND THE GENERAL POPULATION IN CANADA (After Merger)

AREA	ANNUAL INCIDENCE PER 100,000	
	General Population	Laboratory Technicians
Ontario	28 (1952-1953)	667 (1952-1954)
Canada less Quebec	69 (1947-1953)	581[a] (1947-1954)

a. Does not include Manitoba.

Although the pitfalls of comparing rates from populations vastly different in size are obvious and were recognized by Merger along with other possible criticisms, the large difference in morbidity rates is certainly indicative of the consideration risk involved in laboratory manipulations with tubercle bacilli. In the Province of Ontario the case rate ratio between technicians and the general population was 28:1 and for Canada it was approximately 8.4:1.

Sulkin and Pike,[24] in 1949, summarized information on 222 laboratory infections with various viral agents. Twenty-one of the infections were fatal. These cases were obtained mostly from literature reports and from personal communications.

In an unpublished study done in my laboratory, 1135 cases of laboratory-acquired illnesses occurring throughout the world during the years 1893 to 1957 were tabulated. These data were taken from over 250 literature references and personal communications. According to the information available, only 167 out of the 1135 infections occurred as a result of known and clearly defined accidents. Of the remaining cases 583 had no known or suspected cause and 385 had suspected causes listed. The breakdown of cases as to cause was:

Cause known - 15 per cent
Cause suspected - 34 per cent
Cause unknown - 51 per cent

Thus in 85 per cent of the cases a definite cause was not established. Table VI shows a breakdown of the specific known causes of infection.

TABLE VI. KNOWN ACCIDENTS RESPONSIBLE FOR 167 OF 1135 LABORATORY ILLNESSES

THE CAUSE OF INFECTION	NUMBER	PER CENT OF 167
Aspiration of infectious fluid through pipettes	44	26.0
Spills from broken tubes, flasks, pipettes, etc.	30	18.0
Self-inoculation with needles and syringes	25	15.0
Trauma or cuts from contaminated glassware or instruments	19	11.0
Accidental sprays from syringes	16	9.6
Bites or scratches from animals or ectoparasites	11	6.6
Known exposure to aerosols	6	3.6
Pus, etc. sprayed during autopsy	5	3.0
Sneezing of infected animals	3	1.8
Blowing on pipettes	2	1.8
Grinding or blending tissues	2	1.2
Centrifuge accidents	1	0.6
Other accidents	3	1.8

Two interesting points are illustrated by this survey. When cases of laboratory-acquired illnesses occurring earlier in the century are compared with more recent cases, there appears to be a higher percentage of infections in which the cause was known in the earlier group. This undoubtedly is due to the fact that microbiologists have gradually altered their techniques through the years, eliminating many of the more obviously hazardous techniques. Another point of interest concerns the incidence of reported laboratory-acquired cases of tuberculosis. Very few cases have been reported in the literature although it is known that this is one of the most frequently occurring occupational diseases among medical workers. In the 1950 Sulkin and Pike survey, in which questionnaires were used, tuberculosis ranked second among bacterial diseases of laboratory origin. Because of the insidious nature of the disease and the difficulty in ruling out infection sources outside of the laboratory, there has been a tendency to "write-off" many such cases as not being of laboratory origin.

To date the largest body of information on laboratory-acquired infectious diseases was published in 1951 by Sulkin and Pike.[1] Data for the study, which was sponsored by the National Institutes of Health, were collected from the literature and through a questionnaire that was sent to almost 5000 laboratories in the U.S. Information on infections occurring during the previous 20-year period was obtained. In all, 1342 cases were included in the analysis. There were 39 deaths, or a case fatality rate of 3.0 per cent.

Tables VII through X summarize some of the survey information collected by Sulkin and Pike. Seventy-eight per cent of the infections occurred in trained scientific personnel. Janitors, clerical workers, and students accounted for the remaining 22 per cent (Table VII). Bacteria, viruses, and rickettsia together were the etiological agents of 92 per cent of the collected cases (Table VIII). A total of 69 different infectious agents were listed as having caused laboratory infections. Only 215 of the 1342 cases (16 per cent) resulted from known laboratory accidents. Accidents involving the needle and syringe and accidants resulting in the spilling or spattering of viable organisms accounted for almost one half of the known accidents (Table IX). Table X shows the distribution of 1127 laboratory infections for which no known accident was recorded.

TABLE VII. TYPES OF PERSONNEL INVOLVED IN 1286 LABORATORY INFECTIONS (After Pike and Sulkin)

PERSONNEL	NUMBER	PER CENT
Trained Scientific Personnel	1005	78
Janitors, etc.	132	10
Clerical	86	7
Students	63	5

TABLE VIII. AGENTS RESPONSIBLE FOR 1334 LABORATORY INFECTIONS (After Pike and Sulkin)

AGENT TYPE	NUMBER	PER CENT
Bacteria	773	58
Viruses	261	19
Rickettsia	200	15
Fungi	61	5
Parasites	39	3

TABLE IX. SOURCES OF 215 LABORATORY INFECTIONS RESULTING FROM KNOWN ACCIDENTS (From Sulkin and Pike)

SOURCE	NUMBER	PER CENT
Needle and Syringe	57	26.5
Spilled or Spattered Viable Organisms	46	21.4
Injury with Broken Glass, etc.	34	16.0
Pipetting	33	15.4
Bite of Animal or Ectoparasite	32	14.9
Centrifuge Accident	6	2.8
Not Indicated	7	3.3

TABLE X. DISTRIBUTION OF 1127 LABORATORY INFECTIONS IN WHICH KNOWN ACCIDENTS WERE NOT RECORDED (After Sulkin and Pike)

WORK CATEGORY	NUMBER	PER CENT
Worked with Agent	274	24
Clinical Specimens	175	16
Aerogenic	173	15
Contact with Infected Animals and Ectoparasites	139	12
Autopsy	98	9
Handled Discard Glassware, etc.	20	2
Not Indicated	248	22

C. STUDY FELLOWSHIP RESULTS

The problem of obtaining information on past laboratory-acquired illnesses was the most delicate aspect of the study. Most laboratory directors were not eager to discuss this subject, particularily in the presence of their staff members or laboratory technicians. It was in private conversations that most information was obtained. In ten laboratories more or less complete information on laboratory illnesses was obtained. In 37 laboratories very little or no information was given. It is perhaps of some significance that 15 directors offered information not about their own laboratories but about illnesses which had occurred in other laboratories. Thirty-seven laboratory directors gave general but not specific information on their laboratory infections.

In spite of these difficulties I was able to determine that 77 of the 102 laboratories surveyed had had infections. A total of 426 specific illnesses distributed among 31 diseases were recorded from 65 laboratories (Table XI). Not counted in this tabulation were twelve laboratories at which I was told that there had been "many" or "some" laboratory infections. Tuberculosis was by far the most frequently occurring infection, followed by Q fever, brucellosis, psittacosis, and tularemia. The infections listed are, for the most part, cases in which there were clinical symptoms of the disease. Only occasionally did laboratory directors look for inapparent or subclinical infections. The case fatality rate for the 426 illnesses was 4.0 per cent. This is close to the 3.0 per cent fatality rate in the Sulkin and Pike survey. To develop more information on the laboratory-acquired illnesses, each of the 102 laboratories included in the study was placed in one of the following groups according to its principal activity:

1. Commercial or private laboratories - these were mostly laboratories of corporate or privately owned drug firms.
2. Part of an educational institute - these include all educational institutes whether privately owned or owned by the state or government.
3. Noneducational, government or state institutes - these were primarily diagnostic centers, research institutions, and government or state serum institutes.

Table XII shows that noneducational, government, and state institutes, although representing only about one third of the total, were responsible for 64 per cent of the laboratory-acquired illnesses. Furthermore, as the last two columns illustrate, the relative number of infections per laboratory was higher for the government and state institutes than for educational or privately owned laboratories.

These findings are clarified, in part, by the data presented in Table XIII, in which an accounting has been made of the relative number of persons employed and "at risk" in the three types of laboratories. It is evident that although only slightly more than one third of the laboratories were noneducational, government, or state institutes, they accounted for greater than one half of the total number of laboratory employees and for more than 50 per cent of those that were "at risk."

Another significant aspect is apparent when one considers the relative number of infectious agents used in the laboratories. By tabulating the number of different agents used in each laboratory it was possible to estimate the relative position of the three types. Setting the use frequency in commercial laboratories at "one," it was found that following relationship existed:

Relative Use of Infectious Agents in Three Laboratory Types	
Commercial or private laboratories	1.00
Part of an educational institute	1.16
Noneducational, government, or state institutes	1.85

TABLE XI. FREQUENCY OF LABORATORY-ACQUIRED ILLNESSES IN 65 LABORATORIES IN 18 COUNTRIES

DISEASE	NUMBER OF CASES
Tuberculosis	173
Q fever	96
Brucellosis	26
Psittacosis	25
Tularemia	14
Diphtheria	12
Toxoplasmosis	11
Typhoid fever	8
Vaccinia	6
ECHO virus infections	5
Typhus fever	5
Russian spring-summer encephalitis	4
B-virus infections	4
Newcastle disease virus infections	4
Coccidioidomycosis	3
Streptococcus infections	3
Hepatitis	3
Dysentery	3
Choriomeningitis	3
Salmonellosis	3
Influenza	2
Virus encephalitis	2
Smallpox	2
Venezuelan equine encephalitis	2
Plague	1
Mumps	1
Herpes	1
Trachoma	1
Whooping cough	1
Syphilis	1
Tetanus	1
TOTAL	426

TABLE XII. LABORATORY ILLNESSES ACCORDING TO THE TYPE OF LABORATORY INVOLVED

LABORATORY CLASSIFICATION	PER CENT OF TOTAL LABS	PER CENT HAVING LAB ILLNESSES	PER CENT OF TOTAL NUMBER OF ILLNESSES	ILLNESSES PER LABORATORY	
				1	2
Part of an Educational Institute	44	53	25	2.28	4.29
Noneducational, Government, or State Institutes	35	75	64	7.22	9.63
Private or Commercial	21	62	11	2.19	3.53

1. Based on total number of laboratories in each category.
2. Based on number of laboratories in each category that had listed infections.

TABLE XIII. RELATIVE NUMBER OF EMPLOYEES AND THOSE "AT RISK"

LABORATORY CLASSIFICATION	PER CENT OF TOTAL LABS	PER CENT OF TOTAL EMPLOYEES	PER CENT OF TOTAL "AT RISK" EMPLOYEES
Part of an Educational Institute	44	15	17
Noneducational, Government, or State Institutes	35	57	55
Private or Commercial	21	28	28

Thus the noneducational, government or state institutes used, on the average, almost twice as many infectious agents as were used in commercial laboratories. Not reflected in this analysis, of course, is any comparative information on the frequency with which infectious agents were used or the amounts of infectious materials handled. In general, infectious operations at laboratories which were a part of educational institutions were on a much smaller scale than were found in the other two types.

Table XI, in this chapter, listed the frequency of the various diseases found to have occurred among laboratory personnel. Although these undoubtedly are somewhat a function of the types of disease organisms used in the laboratories in years past, it would appear significant to compare the types of infectious agents now being used with the types of past infections. This appears in Table XIV. In the first column the relative frequency of laboratory illnesses is given as the per cent of the total. The second column gives the per cent of all the laboratories in which that particular etiological agent was being used. Figures have been included for two diseases for which no infections were reported. One would not, of course, expect correlation of the two columns of figures since it is impossible to include the many variables which may determine or influence the hazard situation. In several cases, however, it would seem appropriate to comment on the comparative figures. Tuberculosis infections were more frequent than any other, and the causative organism was used more frequently in the laboratories than any other single infectious agent. Q fever was used in only nine per cent of the laboratories but caused 22.5 per cent of the infections. A surprising result was the low frequency of brucellosis infections, although the agent was handled in 20 per cent of the laboratories visited.

In 59 (14 per cent) of the 426 laboratory illnesses a known accident was said to have preceded the illness. Therefore, essentially 86 per cent of the causes had not been established. This information is approximately what would have been expected from past surveys. Table XV summarizes other available data on "causes," along with the above information for comparison. It is important to contrast the causal information on infectious hazards with those resulting from mechanical or chemical injuries as listed on the bottom line.

A tabulation of the known causes among the 426 infections is presented in Table XVI. Self inoculation caused about one third of these infections, followed in order by leaking aerosol chambers, cuts and bruises, centrifuge accidents, and sprays from syringes. In view of the large number of laboratories (62 per cent) who allowed oral pipetting, it was surprising that this procedure caused only two infections. Note that three illnesses were due, in part at least, to the failure to administer the usual vaccines.

In addition to those illnesses for which there was a known cause, a number of laboratory directors listed operations or activities which they felt might have been responsible for illnesses (Table XVII). It is interesting that 28 of the 35 refer to operations which probably could have been conducted in a ventilated safety cabinet.

This survey has shown that, among 65 infectious disease laboratories, in 18 countries there were at least 426 laboratory-acquired illnesses within recent years, almost seven infections per laboratory. Furthermore the causes of these infections were known for only 14 per cent. Of these, self-inoculation accounted for almost one-third. Two points relative to this survey should be emphasized: (a) Although 65 laboratories supplied data on laboratory illnesses, only ten gave a complete account. (b) Not included in the calculations are illnesses occurring in 12 laboratories at

TABLE XIV. COMPARISON OF FREQUENCY OF LABORATORY ILLNESSES WITH USE OF THE CAUSATIVE AGENT

DISEASE	LABORATORY INFECTIONS, Per Cent of Total	PER CENT OF LABORATORIES USING AGENT
Tuberculosis	40.6	58
Q fever	22.5	9
Brucellosis	6.1	20
Psittacosis	5.9	10
Tularemia	3.3	5
Diphtheria	2.8	21
Toxoplasmosis	2.6	4
Typhoid fever	1.9	19
Vaccinia	1.4	10
ECHO virus infections	1.2	14
Typhus fever	1.2	9
Russian spring-summer encephalitis	1.0	8
B-virus infections	1.0	1
Newcastle disease virus infection	1.0	3
Coccidioidomycosis	0.7	2
Streptococcus infections	0.7	19
Hepatitis	0.7	3
Dysentery	0.7	4
Choriomeningitis	0.7	2
Salmonellosis	0.7	29
Influenza	0.5	5
Virus encephalitis	0.5	-
Smallpox	0.5	4
Venezuelan equine encephalitis	0.5	3
Plague	0.2	2
Mumps	0.2	3
Herpes	0.2	3
Trachoma	0.2	1
Whooping cough	0.2	1
Syphilis	0.2	-
Tetanus	0.2	13
Poliomyelitis	0	20
Staphylococci infections	0	29

TABLE XV. KNOWN AND UNKNOWN CAUSES OF LABORATORY-ACQUIRED ILLNESSES

SOURCE	PERCENTAGE	
	Known Cause	Unknown Cause
Review of 1135 published cases, world-wide	15	85
Sulkin and Pike survey of U.S. (1951)	16-20	84-80
U.S. Army Biological Laboratories		
Safety Division reports, 1950-56	30	70
Supervisor's written reports, 1953-56	33	67
Exhaustive investigations of cases (1955-57)	35	65
Present study in 18 countries	14	86
U.S. Army Biological Laboratories		
Mechanical and chemical lost-time injuries	100	0

TABLE XVI. KNOWN CAUSES OF 59 OF 426 LABORATORY ILLNESSES

TYPE OF ACCIDENT	NUMBER OF ILLNESSES
Self inoculation	20
Leak from an aerosol chamber	8
Cuts or bruises from glassware or equipment	6
Centrifuge accident	5
Spray from syringe	5
Animal bites or scratches	3
Failure to immunize	3
Tissue blendor	2
Oral pipetting	2
Sonic vibrator	1
Broken lyophilizing ampoule	1
Animal spat in face	1
Stopper jumped out of tube	1
Suicide	1
Per cent of illnesses resulting from known accidents	13.84

TABLE XVII. OPERATIONS SUSPECTED OF CAUSING 35 OF 367 LABORATORY-ACQUIRED ILLNESSES OF UNKNOWN ORIGIN

OPERATION OR ACTIVITY	NUMBER OF ILLNESSES
Working with organism on table top	12
Sloppy techniques	6
Handling or autopsy of infected animals	5
Inoculating animals, birds, or eggs	3
Eating and smoking in laboratory	2
Preparing viral antigens	1
Cleaning laboratory rooms	1
Dishwashing	1
Doing slide agglutinations	1
Failure to wash hands	1
Contaminated laundry chute	1

which the specific number or type of infections were not supplied. These included cases of brucellosis, diphtheria, ECHO virus infections, influenza, mumps, toxoplasmosis, tuberculosis, typhoid fever, and typhus fever. Therefore, it can be assumed that the number of illnesses counted was considerably less than the actual number.

The importance of maintaining good records of past illnesses was illustrated in one laboratory whose director had used the information shown in Table XVIII, as a justification for requesting funds for a new building and later for additional safety equipment. It will be seen that during approximately 15 years there were 40 laboratory illnesses and relapses. Although approximately 100 persons were employed in the laboratory, not over 20 to 25 of them were exposed in any way to bacterial pathogens. This would indicate an average of about 2.66 infections per year and a lost-time rate per million man hours of approximately 50. (The lost-time accidant rate for the U.S. Steel Corporation is 1.00) In 1953 the laboratory moved into a new building with considerably better safety facilities, but with no cabinets for bacteriological operations. It is possible that those illnesses in Table XVIII listed for 1953 and 1954 were a result of operations in the old facilities. And, of course, all of the relapses of tuberculosis patients may have been from infections originally contracted in the old facilties. It is significant that most of the tuberculosis cases listed were not associated with known laboratory accidents.

Another significant point in this laboratory was that there had been no viral illnesses, although Russian spring-summer encephalitis, louping ill, ECHO, poliomyelitis, adeno, and other viruses had been in use and more people were "at risk" with viruses than with bacterial agents. All viral operations, however, were carried out in ventilated cabinets. There can be

TABLE XVIII. LABORATORY ILLNESSES AT A EUROPEAN LABORATORY

YEAR	PULMONARY TB				DIPHTHERIA		PARATYPHUS		DYSENTERY		TOTALS	
	Initial Cases		Relapses									
	No.	Days Lost	No.	Days Lost	No.	Days Lost	No.	Days Lost	No.	Days Lost	No.	Days Lost
1944					1	-			2	30	3	30
1945					1	234					1	234
1947[a]	1	-			4	314					5	314
1949	1	188									1	188
1950	2	272									2	272
1951	4	630									4	630
1952	3	231	1	490							4	721
1953	2	-									2	-
1954	3	1078	2	947							5	2025
1955			1	245							1	245
1956	1	313	1	197			2	162			4	672
1957			1	131			3	87			4	218
1958	1	87	1	61							2	148
To May 1959			2	-							2	-
TOTALS	18	2799	9	2071	6	548	5	249	2	30	40	5697

a. No illnesses in 1946.

little doubt, in this case, of the protection offered by the use of ventilated cabinets. In fact, having reached a similar conclusion, the director had requested funds for cabinets and other safety devices for the bacteriological laboratories.

As correlative to the instances of laboratory outbreaks of disease reviewed earlier in this chapter, two unpublished outbreaks occurring in European laboratories can be added. In one, 15 clinical cases of Q fever developed among approximately 75 employees in a three-story laboratory building. It was felt that the infections were due to the use of "sloppy techniques" by a laboratory worker who was making a live antigen preparation which contaminated the air of the building. Q fever antigen is no longer prepared at this institute.

In the other outbreak, occurring in 1946, an epidemic of Q fever involved 60 persons in a tropical disease institute. Antibiotics were not readily available and some of the illnesses were severe. Visitors to the building and construction workers were infected as well as laboratory personnel, doctors, and the director of the institute. Although no detailed investigation was made, it was felt that the building air became contaminated through the use of a centrifuge during the preparation of Q fever antigen. This institute also stopped all operations with this infectious agent.

It is difficult to prevent infectious agents from reaching human hosts because these microorganisms are not seen with the naked eye, they are odorless and tasteless, their escape is often difficult to detect, the susceptibility of their hosts varies and the illnesses they cause are usually preceded by an incubation period. Still other factors which cloud the picture are:

1. The innate ability and adaptability of microorganisms to avoid destruction by chemical or physical agents.
2. The expanding list of infectious forms, particularly viruses, which have been discovered.
3. The increased number and widely varied types of manipulative laboratory tests in which the microorganisms are used.
4. The classical attitude of personal sacrifice among medical and laboratory workers.

In this chapter, in the distribution of laboratory-acquired infections according to agent type, no consideration has been given to the number of susceptibles engaged in work with each type. However, it is probable that more bacterial agents were handled in the laboratories studied than were viruses and rickettsiae and that viruses and rickettsiae caused relatively more infections. Fatalities, with viral and rickettsial infections have been more frequent than with other agents. And it is with these groups, of course, that less general knowledge exists concerning modes of disease transfer. In adition, there is every indication that in the future more work will be done with viral agents than with bacterial agents.

From an examination of reports and surveys of laboratory-acquired illnesses, it is apparent that the hazard of acquiring infectious disease is a real and sincere problem to persons handling pathogenic agents. The problem exists as well, and is more insidious, for persons handling medical specimens for diagnostic purposes where the nature of the infecting organism and its concentration may be unknown.

From the data showing the most frequently occurring techniques or procedures which cause laboratory illnesses, it is a relatively simple matter to institute corrective and protective measures against infections of known cause through the use of alternate procedures, by the use of equipment designed to eliminate specific hazards, or by training personnel to exercise more care in certain manipulations. Corrective procedures for infections whose cause is not known is more difficult. Observant scientists have gradually ferreted out specific causes for some infections in the "unknown" group, but the remainder must depend for logical explanation and subsequent corrective action on the results of quantitative studies of laboratory hazards which have been published within the last 15 years.

III. LABORATORY ORGANIZATIONS, FUNCTIONS AND PERSONNEL

A. TOPOGRAPHY OF THE INFECTIOUS DISEASE LABORATORY

Microbiological safety can be divided into two broad elements. One element includes the physical and procedural aspects of laboratory work and the other has to do with the people who manage the laboratories and those who are subjected to microbiological risks. Referring specifically to people who manage or who work in infectious disease laboratories, one can study the "human elements" involved by observing characteristics of workers in general and comparing these with the traits of persons employed in laboratories. While such a study would certainly be valuable in any loss prevention program for laboratories, full treatment of this aspect is beyond the scope of this report. In this chapter and in Chapter IV, observations and calculations relating specifically to laboratory personnel, their functions, and their management will be presented.

It was the German physician Rudolph Virchow who, in 1848, emphasized the important principle that the steps taken to promote health and combat disease must be social as well as medical. To the extent that this is true in the prevention of accidents and disease in the laboratory, it is necessary to attempt to understand and analyze some of the features of the social topography of the laboratory.

Laboratory workers throughout the world who are exposed in their work to infectious agents are employed primarily in educational, government, municipal institutions, and profit-making organizations. Educational institution laboratories are, in the main, less well off financially than other types. Since a substantial block of those exposed to infectious agents work and live in a campus or university society it may be well to examine this social climate as it exists in various countries.

Immediately, one factor reveals itself with distinct clarity. This is the esteemed position that the foreign professor, doctor or scientist holds in his own society. It is true, I believe, that foreign scientists as compared with North American scientists, hold positions of much greater formal and informal power within their own circles. Furthermore, as a result of this, research and laboratory units tend to be autocratic.

The social position of the foreign scientist is revealed in many ways. Medical students in some countries stand at attention when the professor enters and leaves the lecture room. The professor's or scientist's office is usually elegant, even though his laboratory may be poorly equipped. Laboratory workers are usually careful not to refute or contradict statements or opinions expressed by their superiors. The senior scientists are usually afforded greater freedom in having more than one source of income. Other special privileges for the scientific group were not uncommon. Steam bathrooms for professional personnel, a log fireplace in the professor's office, and the use of laboratory workers as chauffeurs and doormen are examples.

Another important point is, "Who is considered to be a scientist?" In the United States one finds bacteriologists and microbiologists with only Ph.D., M.S. or even B.S. degrees. Most foreign countries require education in medicine for these positions and the term bacteriologist or microbiologist usually refers only to the medically qualified person. Workers with lesser degrees or with various certificates are called technicians. The exact position of the technician is important in understanding the social climate. Laboratory workers with degrees or training equivalent to the M.S. or Ph.D. are often referred to as chief technicians and these people stand on a reasonably high rung of the social ladder. This is particularly true in Great Britian where highly trained medical technicians are few. However, with the exception of the chief technician, in general, in foreign laboratories, quite a social gap seems to exist between the scientists and other laboratory personnel. In Japan and Greece the gap was extreme. It was closest in England, Australia, and the Scandinavian countries.

Technicians in foreign countries are more likely to be licensed and to belong to an organization of technicians than are technicians in the U.S. In foreign countries the word "technician" has a slightly different meaning than in this country. In the U.S. many laboratory people with M.S. or Ph.D. degrees would prefer not to be called technicians, but their foreign counterparts are more often proud to have achieved technician status.

Another observation regarding the relationship between scientists and technicians was made. Because the scientist is usually medically qualified, he often acts as physician for the persons working for him and the students under him, treating and administering, or giving advice on medical problems, including occupational illnesses. Thus one sometimes finds a definite doctor-patient relationship. The important aspect of this is the closed-circuit effect. The physician assigns the work, establishes the procedures to be followed (including those used for personnel protection), makes occasional checks on the health of his workers, and sometimes treats occupational illnesses that occur. Thus laboratory infections are often more or less "within the family."

B. SAFETY ASPECTS OF LABORATORY ORGANIZATION AND MANAGEMENT

In the following paragraphs an attempt is made to list and analyze observations which may help to define the position of the organization and management systems in the microbiological laboratories included in the study. Some indications of the feelings of laboratory directors toward microbiological safety were evident early in the study at many laboratories. Other observations were drawn from various events which took place during visits or from interviews with scientists and technicians.

At those institutions where I was scheduled to present a lecture, the director or his staff had almost always made advanced arrangements for the presentation. In some laboratories the director had merely reserved the

lecture hall and invited his employees, and students to attend. More frequently however, there was some type of advanced publicity, members of other laboratories were invited, and often some type of luncheon was held before or after the lecture. On several occasions press interviews followed the formal presentation.

Laboratory directors frequently made other preparations for my visit. Some had prepared formal outlines of their safety activities for review and discussion, but more often current safety problems were listed for discussion. At 32 of 102 laboratories the director or his staff had made obvious preparations for my visit by staff discussions, printed notices, or by cleaning or painting laboratory facilities. Laboratory directors in general were more interested in discussing future plans or present activities than past events.

In 86 per cent of the laboratories the director contributed a significant amount of his time to personal conversations and tours of his laboratories. The remaining 14 per cent left the orientation in the hands of subordinates (usually the assistant director) after the initial introductions were made. At 72 per cent of the laboratories I was allowed to hold discussions with other staff members, technicians, and workers. However some directors (28 per cent) seemed to prefer that I talk only to them or their immediate staff and not to lower level employees.

At each laboratory I recorded my observation of the willingness of the director or his assistant to enter into discussions on microbiological safety. In the majority of instances, 64 per cent, the director seemed eager to discuss specific technical aspects of laboratory safety. This was in part due to the fact that many directors had certain problems in this area with which they hoped to get help. Twenty-one per cent of the laboratory directors seemed willing to discuss safety or other research, while 15 per cent seemed determined not to discuss microbiological safety and expressed very little interest in problems related to it. In 80 per cent of laboratories the scientific staff seemed interested in problems of laboratory safety.

In general it may be stated that the relationship between employers and employees is more formal in foreign countries visited than in the U.S. This can be illustrated in several ways. For example, in eight of 12 U.S. laboratories the director and his staff shared common dining facilities with the laboratory personnel. By contrast, only eight out of 31 foreign laboratories had common eating facilities. In 14 of 31 foreign institutions the staff had a private dining room and in nine instances special table service was normally provided. In several foreign laboratories separate tea or coffee rooms were provided for three social classes; the staff, the technicians, and such laboratory workers as animal caretakers, dishwashers, and janitors.

By studying the organizational structures of the laboratories it was possible to make a subjective separation according to the type of organization. Forty-two per cent of all laboratories visited tended to have an autocratic type of organization. This observation was confirmed by questions regarding how decisions were made. In 43 per cent of the laboratories it was indicated that the administrative head made all of the decisions. In 39 per cent, decision making responsibilities were delegated, and in 18 per cent, decisions were arrived at by the group action of the scientific staff.

The following observations were made regarding the organizational structures in the 102 laboratories:

1. Organizational lines were sufficiently strong to allow full flow of information (55 per cent) and authority (66 per cent).
2. Organizational lines were sufficiently defined (57 per cent).
3. There was some evidence of an informal organization at work (25 per cent).

During discussions with laboratory staff members and scientists it was possible to note certain complaints. These are tabulated below:

Nature of Complaint	Per Cent of Laboratories
Supervision	7
General working conditions	24
Salaries	19
Money for equipment	24
Money for travel	10

The relative frequency of complaints was highest in Australia and Germany, where the most common discomfiture concerned money for the purchase of laboratory equipment. Those complaints classified as "general working conditions" usually referred to inadequate safety measures. "Supervision" complaints alluded to the autocratic nature of the laboratory organizations. Salary complaints were frequently heard in those countries where scientists often hold more than one job.

Information on laboratory management also was obtained by asking directors and scientists how disciplinary problems with technicians and workers were handled. Usually a theoretical example was used to obtain the reaction of the supervisors. As an example, the scientist would be asked what action would be taken if a technician consistantly refused to use some safety device such as a pipettor. In the 102 laboratories the indicated approach to discipline problems was approximately as follows:

Strict and highly formal - 19 per cent
Firm - 45 per cent
Easy - 36 per cent

It would appear that in the majority of the laboratories (64 per cent) strict or firm measures were taken to assure conformity to established procedures. In several instances laboratory directors indicated that they had discharged technicians on the spot for disobeying procedural regulations.

Technicians and laboratory workers were generally less well informed about laboratory hazards than their supervisors. In only 39 of 102 laboratories did the workers appear to have a valid concept of or feel a responsibility for safety. Workers in 14 laboratories indicated that they knew of existing hazardous procedures but were hesitant to insist on changes. In the remaining 31 laboratories, workers simply did what they were told and left all matters concerning safety to the supervisor.

The attitude of management toward technicians and laboratory workers varied widely. In 21 per cent of the laboratories the director or scientists felt that caution should be exercised in discussing laboratory hazards with technicians in order not to frighten them.

Based on the information collected, a classification was made of those laboratories in which management was considered to have a valid concept of its safety responsibilities. The "valid concept" can be considered to be those employer-employee relationships generally found in loss prevention programs in enlightened U.S. industries. In only 43 per cent of the laboratories did management display evidence that it had a valid operating concept of its safety responsibilities. To explain why this is so becomes a difficult problem. As a group the scientists were interested in laboratory safety (80 per cent) and from the practical viewpoint they were faced with safety problems. It would seem that many laboratory managers were torn between modern sociological demands and old customs and operating habits. At any rate the observation that 57 per cent of the laboratories were not managed according to a valid modern concept of safety is supported by the following observations:

1. 65 per cent of the laboratories displayed no real knowledge of basic accident and injury prevention principles.
2. 69 per cent had no active and directed safety program.
3. In 60 per cent it was clear that in the past safety considerations had not been a part of technical planning and was subordinate to other considerations.
4. In 36 per cent the director felt little or no responsibility for laboratory illnesses and accidents among his employees.
5. In 19 per cent management expressed the opinion that laboratory infections were a part of the job. Another 19 per cent felt that it was primarily "sloppy" workers who became infected. However, in 62 per cent the directors or scientists were concerned about laboratory illnesses.

What, then, was the approach taken by the director and supervisors toward laboratory hazards problems? Some general impression can be gained from the following data.

In the majority of instances (71 of 102 laboratories) the director or his assistant could offer more complete information on past laboratory safety performance in his own organization than could other members of the organization. In 67 per cent of the laboratories the scientists felt that both safety equipment and good techniques were necessary to avoid laboratory infections. However, in 26 per cent it was felt that only good, careful technique was required.

When questioned about action which would be taken in case of an existing and obvious laboratory hazard, (assuming that corrective action would involve the expenditure of funds) institute directors and supervisors answered as follows:

1. Would do everything possible to make corrections - 49 per cent
2. Would try for some improvement - 13 per cent
3. Expense usually prevents correction - 16 per cent
4. We have got along thus far without change - 22 per cent
5. Everything possible has already been done - 1 per cent

That budget considerations play a large role in laboratory safety is indicated by the fact that when asked about financial aspects 53 per cent of the laboratory managers suggested that safety could be improved if it were not for monetary limitations.

Laboratory directors and supervisors were asked to react to the suggestion that human factors may play an important role in accident prevention. In 46 of 102 instances a negative response was received. Forty-nine persons felt that the problem should be further investigated.

During inspections in 44 of 102 laboratories, the director of his staff pointed out procedures or equipment which they believed to be hazardous. At 65 per cent of the institutes I was asked to point out equipment or procedures which I considered might create risks. Six laboratory chiefs made on the spot corrections of unsafe acts or equipment.

Substantial evidence exists to prove that common laboratory techniques frequently create aerogenic contamination. In 34 per cent of the laboratories, I felt that the scientific and management personnel had a reasonably good understanding of this phenomenon. The remainder were not adequately informed on this subject. As one laboratory director stated, "Everything that is required for laboratory safety can be found in current textbooks on microbiology." This assumption, unfortunately, is not correct.

In 12 of the 102 laboratories, management level personnel set bad examples for others while conducting me through their facilities. As an example, at one institute I was taken first into the infectious tuberculosis laboratory and then to the laboratory producing Calmette-Guerin bacillus vaccine (BCG) without changing clothes or shoes. In both laboratories all operations were carried out on the table top rather than in ventilated cabinets.

C. LABORATORY FUNCTIONS

In many European educational institutions it is characteristic that the duties of the teaching staff include the operation of a diagnostic laboratory service as well as lecturing and carrying out research. In some laboratories other functions also fall under the responsibility of the teaching staff. For example, the operation of blood-alcohol laboratories for the police department and the production of certain diagnostic reagents is a function of the bacteriological departments of some European universities. A number of scientists were outspoken about this situation, justly stating that not enough of their time could be devoted to any one duty. It was apparent also that this often resulted in poor supervision of infectious laboratory operations. However, in at least 16 institutions the director implied that the funds derived from the laboratory services were essential in order to maintain the department. This situation is not typical of laboratories in the U.S. and Canada. In England and Scotland the national medical service apparently pays the salaries of the medical staff of the bacteriology departments. In Scotland, each of the bacteriology departments of the several universities provides the public health service and medical diagnostic service for a particular area.

Economic conditions are usually responsible for multiple function laboratories, but local customs also play a part. In many small countries it is logically assumed that the bacteriological laboratory is to handle all things bacteriological. Consequently there is not as much evidence of specialization of function as in this country.

Almost all laboratories included in this study carried out two or more functions. The relative frequency was:

Laboratory Function	Per Cent
Research	84
Teaching	50
Medical or hospital diagnosis	46
Public health laboratory services	36
Production of biologicals	18
Animal production	2

The number of microbiological laboratories responsible for two, three, four, or even five separate functions was relatively high in some countries. As indicated above this is significant because when scientists and laboratory directors are called upon to serve in a number of capacities, too little time is available for each function. As the functions and responsibilities of supervisors are increased there is less administrative supervision over workers handling infectious materials.

Table XIX shows the percentage of the laboratories visited in each country which were engaged in the functions listed. It is apparent that, on the average, laboratories in most countries served for more separate

functions than those surveyed in the U.S. By Adding the figures for each country one obtains a figure which represents the frequency of multiple purpose laboratories. This is shown in Table XX.

TABLE XIX. FUNCTIONS OF LABORATORIES BY COUNTRY

COUNTRIES	PER CENT OF LABORATORIES CARRYING OUT INDICATED FUNCTIONS					
	Research	Teaching	Medical Diagnosis	Public Health Service	Biologics Production	Animal Production
Australia	89	56	56	11	11	
Canada	80	60	40	60	40	
England	87	33	27	20	33	13
Finland	80	40	40	40	40	
Germany and Austria	100	73	64	73	18	
Greece	25	25	100			
Netherlands	100	50	100	50	50	
Norway	83	67	17	50	17	
Scotland	80	80	80	60		
Sweden	100	56	78	56	11	
U.S.	75	40	28	12	8	
Japan, Italy, Portugal, France, Denmark, and Switzerland	100	50	33	83	33	

TABLE XX. RELATIVE FREQUENCY OF MULTIPLE PURPOSE LABORATORIES IN 18 COUNTRIES

COUNTRIES	RELATIVE FREQUENCY
Netherlands	350
Germany and Austria	328
Sweden	301
Scotland	300
Japan, Italy, Portugal, France, Denmark, and Switzerland	299
Canada	280
Finland	240
Norway	234
Australia	223
England	213
U.S.	164
Greece	150

Although infectious or toxic agents were used in many types of laboratory operations, they were most frequently encountered in research work, as shown in Table XXI. Even though 50 per cent of the laboratories were used as teaching facilities, only 12 per cent utilized infectious agents in teaching functions.

TABLE XXI. OPERATIONS INVOLVING THE USE OF INFECTIOUS OR TOXIC AGENTS

FUNCTION	PER CENT OF LABORATORIES USING INFECTIOUS OR TOXIC AGENTS
Research	81
Medical diagnosis	65
Production of biologics	19
Teaching	12
Animal production research	1

Table XXII shows the frequency of use of infectious agents by functions in the laboratories studied in the various countries. In some laboratories infectious materials were avoided entirely in teaching situations. In medical and public health functions infectious agents were encountered more frequently in foreign countries than in the U.S. This can be attributed to two possible factors: (a) a greater degree of specialization in U.S. laboratories and (b) the greater frequency of infectious diseases such as tuberculosis in the population of foreign countries.

Laboratory function can also be defined in terms of the types of infectious microorganisms handled. For the 102 laboratories this classification is as follows:

Bacteriology only, no facilities for viral work - 35 per cent
Capable of doing both bacterial and viral work - 60 per cent
Just beginning to do viral work - 4 per cent
Viral work only - 1 per cent

This classification, of course, does not reflect the relative volume of work with bacterial and viral agents, nor does it indicate the substantial trend toward more viral work.

TABLE XXII. FREQUENCY OF USE OF INFECTIOUS AGENTS BY FUNCTION IN THE DIFFERENT COUNTRIES

COUNTRIES	PER CENT OF LABORATORIES USING INFECTIOUS AGENTS IN THE INDICATED FUNCTIONS				
	Research	Teaching	Medical and Public Health Diagnosis	Biologics Production	Animal Production
Australia	78	11	44	11	
Canada	60	--	100	40	
England	87	7	53	27	7
Finland	80	20	60	40	
Germany and Austria	100	9	91	18	
Greece	25	--	100	--	
Netherlands	100	--	100	50	
Norway	83	--	67	17	
Scotland	80	--	80	--	
Sweden	100	22	78	22	
U.S.	72	20	36	8	
Japan, Italy, Portugal, France, Denmark, and Switzerland	100	17	100	33	

D. LABORATORY PERSONNEL

Variation in size of the laboratories included in the study is indicated by the number of persons employed at each institution. Such a tabulation is shown in Table XXIII. Eleven per cent of the laboratories employed fewer than 10 people while 16 per cent employed over 151. Over 50 per cent employed between 10 and 50 persons.

TABLE XXIII. NUMBER OF PERSONS EMPLOYED IN 102 INSTITUTIONS

TOTAL PERSONS EMPLOYED	PER CENT
less than 10	11
10 - 25	25
26 - 50	26
51 - 100	18
101 - 150	4
over 151	16

The data collected allow a more detailed analysis of the number of persons employed in the laboratories, the relative number of scientists, and estimates of the number who are potentially exposed to infectious microorganisms. These data are presented in Table XXIV. It is to be noted that the term "at risk" is used to designate any potential degree of laboratory exposure. Many laboratory persons who do not directly handle cultures or infected animals are therefore included. Potentially "at risk" janitors, mechanics, and office workers, for example, are included as technicians and others.

Using this method of classification, it was estimated that 61 per cent of the 11,049 employees in the 102 laboratories were potentially exposed to infectious materials. It is worth noting that at one large European laboratory (700 employees) "at risk" personnel were given hazard pay. On the average, the laboratory staff consisted of 15 per cent scientists and 85 per cent technicians and others. Of the total for each group, about the same percentage was potentially exposed to infectious agents; 62 per cent for the technicians and 59 per cent for the scientists. Therefore the typical exposed population in an infectious disease laboratory consisted of 14 per cent scientists and 86 per cent technicians and others.

It is desirable to consider further the relative position of the M.D. or D.V.M. degree person in the laboratories surveyed. As shown in Table XXIV, 6 per cent of laboratory personnel and 38 per cent of the scientists held M.D. or D.V.M. degrees. Scientists more frequently exposed were those

holding B.S., M.S., and Ph.D. degrees or the equivalent. Although 38 per cent of the scientists held medical or veterinary degrees, the relationship varied significantly from country to country, as illustrated in Table XXV. The variation was from 12 per cent for the 25 U.S. laboratories surveyed to 100 per cent in the four Greek laboratories. This is due in part to the fact that Ph.D. degrees in microbiology or bacteriology are not granted by the educational institutions in many countries. Although the customs are changing steadily, it is primarily in the U.S. that a student can obtain an advanced degree in microbiology without attending medical school. Table XXV also indicates, for the separate countries, the per cent of the total laboratory personnel who were classified as scientists. As can be seen, with the exception of Greece, the countries had between 8 and 30 per cent scientists in the laboratories surveyed.

TABLE XXIV. PERSONNEL IN 102 MICROBIOLOGICAL LABORATORIES IN 18 COUNTRIES

Total number persons employed (approx)	11,049
Number of scientists employed	1,661
Per cent of employees who were scientists	15%
Number of scientists with M.D. or D.V.M. degrees	635
M.D. or D.V.M. degrees, per cent of total employees	6%
M.D. or D.V.M. degrees, per cent of total scientists	38%
Number other than scientists employed	9,388
Per cent of employees who were not scientists	85%
Total number of persons "at risk" with infectious agents	6,791
Per cent of total employed at risk	61%
Number of scientists "at risk"	934
Per cent of total persons employed	9%
Per cent of total scientists employed	59%
Per cent of total "at risk" people	14%
Number of technicians and others "at risk"	5,807
Per cent of total persons employed	53%
Per cent of total technicians employed	62%
Per cent of total "at risk" people	86%

TABLE XXV. RELATIVE NUMBERS OF SCIENTISTS AND M.D. AND D.V.M. DEGREE PERSONNEL

COUNTRIES	PER CENT SCIENTISTS IN LABORATORIES	PER CENT SCIENTISTS HAVING M.D. OR D.V.M. DEGREES
Australia	13	30
Canada	10	28
England	19	27
Finland	11	79
Germany and Austria	19	68
Greece	50	100
Netherlands	8	17
Norway	19	98
Scotland	30	42
Sweden	21	66
U.S.	21	12
Japan, Italy, Portugal, France, Denmark, and Switzerland	11	35

IV. THE ADMINISTRATION OF LABORATORY SAFETY

A. A MODEL LABORATORY SAFETY PROGRAM

Laboratory-acquired illness has been a problem since the early days of microbiology and as a result of expanded activity in the field, the discovery of new disease agents, and other factors, laboratory-acquired illness continues to be a problem.

Accurate estimates of the frequency of laboratory-acquired illness are not available. Surveys made in this country and abroad show that approximately 80 per cent of recorded laboratory illnesses are not the result of known accidents and therefore are probably due to escape of infectious agents during routine manipulations.

The science of microbiology in the past has been characterized by a tradition of self-sacrifice by workers in the field, but legal and morale considerations have caused a movement to reduce needless illness due to occupational laboratory infections. (e.g., World Health Organization, American Public Health Association and U.S. Government Agencies.)

Until recently, laboratory accident causes were given little consideration. The infecting microbe was said to be the cause of the illness. The technical error which placed the microbe in a position to infect usually was not considered unless it was an obvious one. Nonetheless a number of such "bad practices" became recognized. Technical research during the last two decades has uncovered a number of additional hazardous procedures so that today we are aware of most of the necessary safeguards. What remains to be done is to encourage the use of the safeguards and to make safety a "way of life" in the laboratory. Among the most important tools available are those of education, training and enforcement. One must be particularly careful, however, that the approaches used are realistic and that they will be effectual.

The microbiological safety problem in its simplest form is one of environmental control. The microbe must be contained in its environment (the test tube, flask, etc.) and the microbiologist must assure himself that he is externalized from the organisms' environment. Although this appears to be straightforward, its possible complexity can be illustrated by the fact that quantities of microbes capable of causing human infection are not readily perceptible in the usual sense. The infecting dose may be odorless, tasteless, and invisible to the naked eye.

From existing evidence it is clear that the heuristic desires of scientists and the technical knowledge of the staff can be integrated with the desired safety approaches only through a well planned and organized safety program. This chapter outlines features which are important in organizing a laboratory safety program. The "model" program is one that may have universal application by selecting only those functional elements

needed for any particular infectious disease laboratory. Next, in this chapter, information collected on the administration of safety in U.S. and foreign laboratories will be presented. As will be seen, one of the principal deterrents to safety in microbiological laboratories is the failure to establish a well-planned safety program.

Figure 3 shows the organizational elements for the "model" safety program. Starting with a common organizational structure, an attempt is made to show how a safety program for laboratories can be integrated into the general organization, what operational elements should be added and what actions by management and employees are required. In a sense the program shown and described has been over-designed, but this has been done purposefully to allow some degree of selection and adaption.

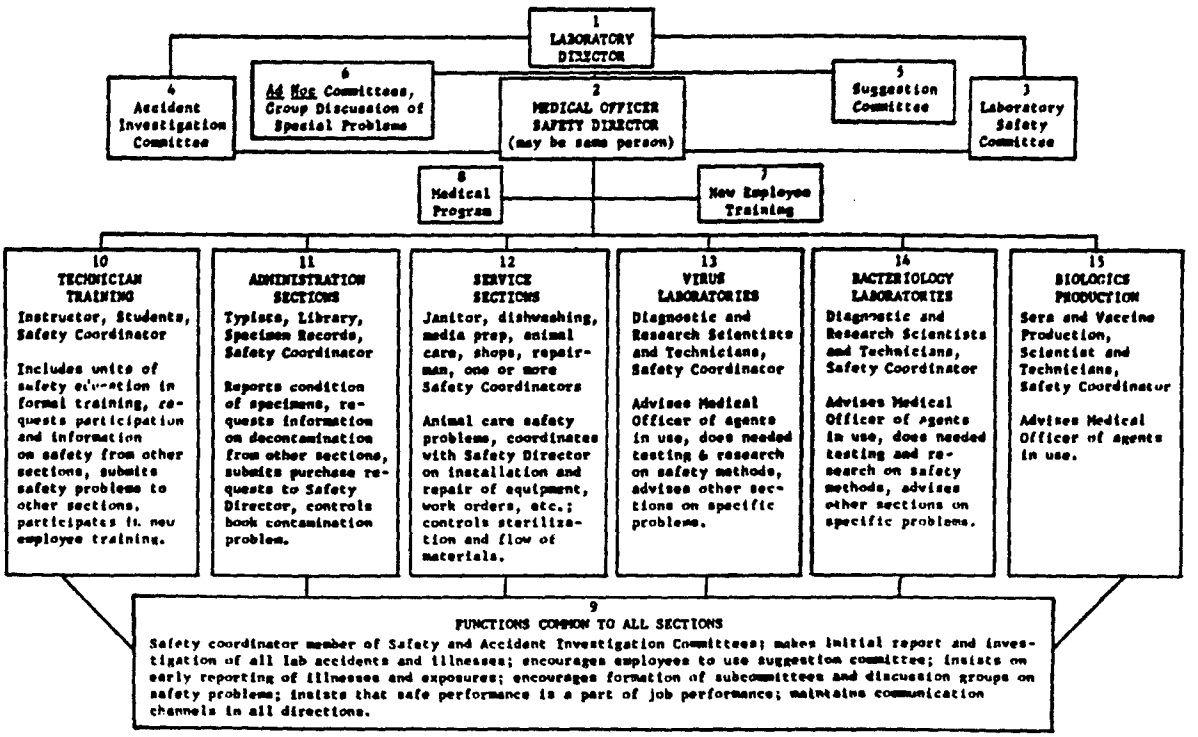

Figure 3. A Safety Program for Infectious Disease Laboratories.

Presented below is a functional outline which is keyed to the organization chart in Figure 3, and which explains each element in further detail.

1. The Laboratory Director

   Must give support and backing to the entire safety program.
   Acts as chairman of the accident investigation committee.
   Appoints ad hoc committees to discuss special problems relating to safety.

Sets up a committee to consider suggestions made by employees.
Attends meetings of the laboratory safety committee, receives and takes action on their reports and recommendations.

2. Medical Officer - Safety Director

Because of the problems of infectious disease and the requirements for vaccination, chest X rays, and physical examinations, most health laboratories should have a full or part-time medical officer. Sometimes the laboratory director also may be the medical officer. More frequently the medical officer also may be the safety director. This is recommended providing the person has sufficient time to perform both functions. At least the safety director should be a person of equal prestige who can work closely with the medical officer and whose academic background is acceptable to the scientists with whom he must work.

The medical officer should be aware of what disease agents are in use in the laboratories, what infection routes are possible, what laboratory manipulations are being carried out, and the best therapeutic methods available. He should treat first-aid cases and injuries with an awareness of the possible contamination of wounds with laboratory microorganisms. He will render a great service if he can train the employees to be constantly aware of their health status and not to overlook minor but often important symptoms which occur early in the course of many diseases.

Ideally, the safety director should occupy a job with little formal power, but should be able to develop sufficient informal power to operate effectively. He is the nucleus of the safety program. While he must have certain specific duties and exercise control over certain risk procedures because they may involve potential epidemic situations, his aim should be to encourage employees at all levels to plan and participate in their own safety program. He should take every step possible to maintain active communication channels between all groups of the organization.

The safety director also

Serves as chairman of the laboratory safety committee.
Serves on the accident investigation committee.
Organizes safety training as a part of the new employee training program.
Assists the technician training instructor in including safety units in the regular curriculum.
Receives and analyzes reports and information on laboratory illnesses, lost-time accidents, first-aid cases, and near accidents.
Reviews work orders, purchase requests, and repair orders.
Organizes safety regulations and directives for approval and publication by the laboratory director.
Conducts periodic inspections of the facilities.

3. Laboratory Safety Committee

If properly organized and effectively maintained, this committee can be an important instrument in maintaining interest in safety. It is important that the laboratory director make known his sincere interest in the committee, that he participate whenever requested, and that he consider carefully all recommendations made by the committee.

The committee should meet at regular intervals, preferably once each month, to consider current safety problems. Members can be formed into work groups or subcommittees to investigate specific problems. Formulation of general and specific safety regulations can be one task of the committee. All recommendations should be sent to the laboratory director for approval and action.

4. Accident Investigation Committee

The laboratory director should use the accident investigation committee to determine causes of accidents and laboratory-acquired illnesses and to recommend corrective action. The committee should include the safety director, the medical officer and other persons who may be able to contribute causal information about any accident or illness under investigation. When enlightened discipline of employees is required, it should be as an entirely separate action by the director and not by the committee. Positive findings of the committee should be put to work by the safety director through the laboratory safety committee.

5. Suggestion Committee

This device often stimulates employees at all levels to contribute to the operation of the organization. Generally many of the suggestions received will concern safety matters. Sometimes a rewards system may be incorporated. In any event a suggestion committee system should be used only after careful study of all ramifications, because if not properly organized and run it may act to the detriment of the safety effort. Obviously the suggestion committee system is more applicable in larger organizations.

6. Ad Hoc Committees

In the field of microbiological safety, the hazard scene is not only partially unknown, but is also subject to change as new disease organisms are discovered and as new diagnostic techniques are introduced. Sometimes these changes can bring about potential laboratory hazard problems about which little is known. At other times it may be only suspected that a potential hazard exists. For example, one might ask: If some human cancer is of viral etiology, as many scientists suspect, are scientists and technicians who handle specimen or research material at risk of becoming infected? If hazard problems can be anticipated, the laboratory director would do well to use ad hoc committees to develop information or recommendations. Outside consultants and specialists in various fields may be utilized.

7. New Employee Training

According to the size of the organization, this may be a formal or informal function. In either case part of the training period should be devoted to acquainting the employee with the safety program and making clear to him his own personal role in the accident and infection prevention endeavor. Furthermore, all new employees should receive this training. Too often it is assumed that people of higher rank entering employment do not need such indoctrination and training.

8. Medical Program

Microbiological safety programs require good integration with the medical activities. Laboratory infections have occurred because someone forgot to vaccinate new employees. Functions of the medical program should include:

Determining that each new employee meets an acceptable standard of health.
Providing periodic physical examinations and chest X rays.
Administration of required vaccines to "at risk" personnal.
Carrying out a testing program to detect inapparent or subclinical infections.
Providing immediate treatment in case of injury or accidental exposure.

9. Functions Common to All Sections

Even though absolute control measures are often necessary, a "personalized" safety program is more desirable. A program in which each employee is aware that efficient and safe actions are an integral part of his job requirements is generally a good program. When continuous safe performance becomes a part of the job goals of individuals, progress in accident prevention should result.

Each section or operating unit should have one or more safety coordinators. This may be a permanent or revolving position, but in either case it should be a part-time assignment to some person in authority at that level. The coordinator serves as a member of the laboratory safety committee and, when requested, on the accident investigation committee.

Functions to be carried out by or through the safety coordinators are:

Making initial reports and investigations of accidents and illnesses.
Collecting information on near accidents and first-aid cases.
Seeing that all safety regulations and directives are followed.
Maintaining communication channels for distribution of information.
Encouraging early reporting of illnesses and exposures.
Making safe performance a part of every job.

10. Technician Training

Laboratories in many parts of the world are assigned the function of training students who wish to become laboratory technicians. Often the central or largest laboratory will operate a training school, which will provide the technicians needed by the laboratory itself and by other laboratories in the area. Inclusion of units of safety education in the formal training program will pay dividends. Management of safety in any situation is much easier if employees do not have to "unlearn" unsafe practices.

11. Administration Sections

A variety of hazards may be encountered by persons working in these sections, not the least of which may be those dangers that arise out of the employees lack of knowledge about "things microbiological." For this reason particular care must be exercised in selecting the safety coordinator for administration sections. A constant danger is that the coordinator or someone else will foster a "fear complex" among these nontechnical employees. The best approach is clear explanation of the hazards in understandable terms with concise recommendations for avoiding exposure. For example, in this manner secretaries who handle laboratory reports, incoming specimens, etc., can usually be taught not to put pencils in their mouths and to wash their hands at appropriate times. The safety coordinator of the administration section can work closely with the safety director in other control measures. Requests for purchase of new laboratory apparatus or equipment, for example, can be routed to the safety director for his approval.

12. Service Sections

According to the size of the laboratory organization, one or more safety coordinators from the service sections may be needed. Some of the safety problems are similar to those in the administrative area. Few of the people will have training in microbiology, so a direct and simple explanation technique must be used to avoid fear of the work. In these sections, more than in any other, the safety director and scientists in the organization should devote time to developing confident and safe procedures among dishwashers, animal caretakers, repairmen, etc. The safety director can operate many routine control measures through the service sections. Installation or repair work orders can be sent to the safety director for his review. Since supplies coming from and going to laboratories involve these sections, check points for adequacy of sterilization can be established.

13, 14, and 15. Laboratory Sections

The organizational division of the laboratory functions may vary. Sometimes research is separated from routine functions, but more often, since the facilities required are somewhat different, the division is made according to scientific specialties such as bacteriology, virology, mycology, and serology. Each sizeable laboratory section should have a safety coordinator.

Through the coordinator an effort should be made to maintain interest in microbiological safety. Participation is probably the principal device to use. Various scientists and technicians should be asked to advise other sections on various matters; certain groups can be asked to do applied research to solve current safety problems. Constant participation followed by recognition will do much to maintain a well integrated safety program. Scientists should be encouraged to design safety into new techniques and procedures which are developed.

B. SAFETY PROGRAMS IN LABORATORIES STUDIED

This section deals with various aspects of the safety programs observed in infectious disease laboratories. An attempt was made to gather details regarding the practices routinely carried out following laboratory accidents and illnesses and the administrative practices taken to prevent accidental loss.

It has been mentioned previously that 64 per cent of the laboratories had had occupational infections and their directors supplied information concerning the number and types of infections. Twelve per cent admitted that infections had occurred but did not state how many, while 24 per cent claimed no infections. Thus 76 per cent of the laboratories had experienced infections among their personnel. In most of these laboratories it was admitted that prevention of infections was a problem of some concern. But in 68 per cent of all laboratories it was felt that laboratory accidents were not a particularly serious problem. This reaction may be in part due to the general lack of correlation of infections with specific accidents, a finding well established by the studies summarized in Chapter III.

Are laboratory accidents inevitable or can they, through correct supervision, be largely eliminated? Among the supervisors in 90 laboratories who responded to this question, 69 per cent felt that prevention was possible. But 69 per cent of all laboratories had no active and directed safety program! In only 29 institutes were records of laboratory illnesses maintained. Only ten laboratories indicated that they keep a written record of past laboratory accidents. In 35 laboratories little or no effort was made to discover the causes of laboratory illnesses. And 88 per cent of the laboratories made no investigations of laboratory accidents.

Formal accident reporting systems were seldom used except in the larger institutions. Employees in 33 laboratories were instructed to report accidents but only 9 of these required a written report. Four laboratories required minor accidents such as cuts and scratches to be reported.

Almost all employees of the institutes visited had some type of monetary compensation available to them in case of occupational injury or disease. Compensation in most cases was the same as that provided in that country for nonlaboratory workers. At 32 institutions (usually those associated

with a hospital) it was indicated that treatment was provided for sick or injured laboratory people. Almost all laboratory directors stated that they gave their employees the benefit of the doubt for compensation purposes if the occupational origin of the disease or injury was in question. In England, Scotland, Sweden and other countries having government sponsored medical services, the occupational aspect of the injury or disease makes little difference since the treatment is provided in any event. It is possible that in individual laboratories the easy availability of medical care has served to de-emphasize the necessity for adequate safety measures.

To present a clear, over-all picture of safety program activities in relation to needs and in accord with projected plans, each laboratory was assigned to one of seven paragraphs which best described the situation and policy indicated by the person or persons in charge. All 111 laboratories visited are included in this analysis. The number of laboratories assigned to each paragraph and the percentage is shown below with the descriptive information.

Paragraph 1: 39 Laboratories, 35.0 Per Cent

In the past, laboratory infections were a substantial problem. Changes have improved the situation, but management feels that much more could be done and/or wishes to obtain information to use for this purpose.

Paragraph 2: 21 Laboratories, 19.0 Per Cent

It is likely that this laboratory has had or will have problems with occupational illnesses. However, management feels that there is little within its power that can be done or that it is willing to do. Consequently there is little likelihood of immediate improvement.

Paragraph 3: 16 Laboratories, 14.4 Per Cent

Laboratory infections are a problem. Little has been done as yet, but management is presently engaged in efforts to reduce future infectious hazards. However, they feel that outside help and advice will be needed.

Paragraph 4: 12 Laboratories, 10.8 Per Cent

Although this laboratory at present has no particular problems with laboratory-acquired infections, future plans for the expansion of the program and/or facilities may create problems. Management is concerned and wishes to obtain information to use in future planning.

Paragraph 5: 11 Laboratories, 11.0 Per Cent

In the past, laboratory infections were a substantial problem. Changes have been made in techniques or equipment that have improved the situation. Management is satisfied with this improvement and, although infectious hazards are still a problem, is satisfied to get along as they have. No future improvements are contemplated.

Paragraph 6: 8 Laboratories, 7.2 Per Cent

This laboratory handles no human pathogens or only "low-grade" pathogens. There is no safety program for infectious hazards and none is needed. No future plans include the use of pathogens.

Paragraph 7: 4 Laboratories, 3.6 Per Cent

Past efforts have been successful in reducing infectious risks. Present facilities and procedures seem entirely adequate; therefore few, if any, future changes are contemplated.

C. POLICIES AND OPINIONS ON SAFETY

How do laboratory workers think and feel about safety? Realistic treatment of this question demands some classification of hazards, since opinions by individuals varied widely. First, it is appropriate to consider those procedural hazards that are well known to most laboratory workers and then to treat those hazards that are real but not as apparent.

Opinions that were expressed to me by technicians in the various countries were about the same in scope and covered a range of viewpoints. The danger of aspirating infectious fluids when mouth pipetting is universally recognized. The same is true of the danger in grinding infectious tissues, flaming contaminated inoculating loops, and self-inoculation with a syringe and needle. The majority of workers at the bench agree that precautionary measures should be taken when carrying out such techniques. However, only a few workers appeared convinced enough of the hazards to employ the recommended safe procedure consistently. The best example of this is mouth pipetting. When the laboratory director did not insist on the use of pipetting devices or when the no-mouth-pipetting rule existed but was not enforced, workers frequently were observed pipetting infectious or toxic fluid by mouth. In this case workers or supervisors often explained that "normally" a pipetting device would be used but that now the volume of work to be done was too great to use the safer and more time-consuming method of pipetting. On the other hand, in laboratories where the director enforced the no-mouth-pipetting rule there were few or no complaints and the technicians appeared to be proud that, in enforcing the rule, the director had a concern for their health and welfare.

Within reasonable limits the views of the workers at the bench level were usually influenced by the opinions and actions of the supervisory scientists. Thus in a number of instances the infraction of a rule was due to the fact that the workers knew that the laboratory director was not firmly convinced of the necessity for the regulation and did not himself abide by it.

Only a minority of laboratory technicians who handled infectious cultures were aware of the inapparent hazards of infectious manipulations (those arising from common procedures such as opening test tubes, transferring liquids, blowing out the last drop from pipettes, etc.). Most laboratory directors had some knowledge of these hazards but few could be classed as well informed. Too many laboratory directors felt that, because of financial or space considerations, there is relatively little that could be done to eliminate the less obvious hazards. Too often they are likely to accept the risk and do what they can to avoid making an issue of the matter. On a number of occasions directors became concerned that technicians would be frightened by a frank discussion on laboratory safety.

In the remainder of this section are recorded the essential elements of statements about microbiological safety made by laboratory directors and supervisors in various countries. The statements are usually not direct quotations, but the central thoughts conveyed to me in conversations with individuals during interviews. These paraphrased statements show the great divergence of opinions that exists. On the one hand it may be said that some laboratory people, in expressing their policies and opinions, are clearly partial to pet theories which, in many instances, have not been substantiated by research in this area. Other pet theories may indeed be true in relation to safety, but the individual may have excluded other equally important phases or assigned exaggerated importance to one theory. On the other hand there is evidence in these statements that some people have devoted considerable time to analyzing infectious hazards problems and in formulating management policies for safety.

Australia

1. We must make every effort to create safe working conditions. The task is difficult because of lack of communications.

2. If you work with infectious materials you are bound to get the disease sooner or later.

3. Infections are usually caused by obvious technical errors.

4. A large new laboratory is to be built and we need all the information we can get on how to set up the safety program.

5. Teaching of correct techniques to students in microbiology needs improvement.

Austria

1. We are worried about possible infections with Russian spring-summer encephalitis virus and badly in need of a vaccine. The most important safety procedure in the laboratory is the frequent decontamination of surfaces.

Canada

1. Retirement of the present director will enable our staff to establish a realistic safety program. The assistant director is keenly aware of responsibilities for safety. Continuous supervision, training and retraining are important. People have been discharged for violating safety rules. The assistant director believes that laboratory directors themselves should be discharged if they have illnesses among their staff and if they are unable to show that any corrective procedures have been made. But laboratory directors badly need a comprehensive manual on microbiological safety.

Denmark

1. Records of illnesses are kept. Safety is considered in the design of buildings and experiments. Our management is sincerely interested in hazard elimination.

England

1. Safety is best worked through a committee who inspects, reports and investigates. There must be good medical support. We have a "rest home" or vacation spot where people who have had accidents or who are physically or mentally exhausted may go for a rest with all expenses paid. Long lists of formal regulations are not necessary.

2. Each senior scientist runs his own safety program. However, precautions must be established to protect workmen, visitors, and outside contractors. Some things are done for "political reasons."

3. "Everyone is doing too much to provide protective equipment and not enough toward eliminating causes." Insofar as laboratory safety is concerned, infectious laboratories may be divided as follows:

   a. Routine - Most jobs can be anticipated and some techniques are done over and over. Therefore good control is possible, providing there is good supervision and planning.

b. Research - Hardest to control because the problems encountered and the techniques required cannot be anticipated.

c. Production - Occupies a position between (a) and (b). Most procedures can be anticipated but they are complicated by a requirement for product protection as well as personnel protection.

Many infection causes can be eliminated by developing alternate techniques. To be continuously successful in a safety program a director must think safety, practice safety, and see that others do the same. In his safety activity, any laboratory director can be placed in one of four categories:

a. Active - Accepts the responsibility for the safety of his people and actively plans and supports the safety program. Sets a good example in his own work and insists on conformity to the established regulations.

b. Passive - Does not care whether or not there is a safety program so long as it is done by others and he is not inconvenienced.

c. Against - Does not believe that time or money should be spent for safety and refuses to consider changes in laboratory procedures. Probably believes that infections are a "risk of the trade."

d. Window Decorator - Institutes some safety procedures or installs equipment without careful thinking or planning for the purpose of impressing others or for some political reason.

In organizing a routine laboratory it is best to use the "one large group" theory rather than the "cellular" theory. In the former all technicians do all the jobs. This produces better team work, it allows the informal organization to function and creates safer working conditions.

4. The chief technician is the safety officer but he has no power and none of his suggestions is used. Cabinets are not necessary. Too much emphasis on laboratory safety will scare people.

5. Two infractions of the no mouth pipetting rule are cause for discharge. Our safety program is based mainly on prevention of infectious aerosols. We prefer that the same techniques be used for pathogens and nonpathogens.

6. Further medical statistics are not needed to prove that laboratory infections are a problem. It is up to the bacteriologists to go into the causes.

7. Waring blendors are not allowed. There is a great need for cheaper and faster methods of sterilizing materials. Japanese B virus mouse brain vaccine is not used because of the danger of untoward vaccination reactions. A section on laboratory safety is to be included in our post-graduate course on bacteriology.

8. Vaccination is the main precaution for work on smallpox.

9. Safety is a committee function but regulations and training programs are also utilized. Each person signs a statement that he has read and understands the regulations and knows that safety responsibility is a part of his job. The "informal organization" has decreed that only the best people are permitted to work with pathogens. This promotes a spirit of pride and team work.

10. Laboratory safety is not a serious problem as long as one handles only a small amount of material at a slow pace. In this case no special equipment is needed. The real hazard is in the human autopsy room.

Finland

1. I will have to consult with my technicians to get details on the laboratory infections.

2. Many laboratories get into trouble when there is a sudden increase in the volume of work. During epidemics of typhoid and diphtheria in this country my laboratory work load was so heavy I didn't even have time to count the laboratory-acquired illnesses.

3. We have built one of the best laboratories in all the world, and we have overcome most problems of laboratory safety.

France

1. Our emphasis is on technician training and supervisory responsibility. We have safety regulations, but the importance of aerosols from laboratory procedures is not well understood.

Germany

1. We must stop oral pipetting because, if we have occupational illnesses, compensation can be denied if mouth pipetting was used.

2. Techniques for safety include immunization, work clothing, laboratory design, laboratory equipment, air and surface disinfection, body hygiene and animal handling. Our aim is to have the best laboratory safety program in Germany.

3. Proper training of technicians is important. Women should not work with toxoplasma.

4. Safety films are good because that is one less lecture I will have to prepare.

5. Frequent washing of hands is important. Infections often occur in new personnel who are not properly acquainted with the work.

6. To prevent infections a gauze mask must be worn.

7. Little can be done to improve safety in our present facilities. We are planning a good program in our future new building.

8. Everyone who works with brucella becomes infected - then we are immune.

Greece

1. We use no measures to avoid infectious risks; "What can one possibly do?"

Holland

1. Our safety program is based on two points, (a) keep the infectious area as small as possible, and (b) use negative pressure cabinets. Records of illnesses are not kept by management. Our building design was copied from NIH. Our employees receive hazard pay. Committees are not used in our safety program. They are only a device for diluting responsibility.

Italy

1. We are not particularly interested in safety programs. When we have a problem, we will then take the necessary steps to correct it.

Japan

1. Human life in this part of the world is very cheap.

Norway

1. As little money is available, safety must be obtained through good techniques without a lot of equipment.

2. Our management realizes that aerosols are produced from many common techniques. Safety testing is carried out to discover hazards, but subsequent corrective procedures are inadequate.

3. The main problem in establishing new laboratories and in maintaining an adequate safety program is obtaining precise information on "how to do" things.

4. We know very little about laboratory safety but are interested in learning. However, we have very little money to spend.

Portugal

1. Funds are very hard to get. We have done nothing about laboratory infections because, in addition to the lack of funds and personnel, we have no information to tell us how.

Scotland

1. Work only with small amounts of infectious material, avoid mouth pipetting and wash your hands frequently.

2. A safety cabinet is needed for infectious work as well as adequate regulations. The conjunctiva may be a route of infection for laboratory people.

3. Disinfection and sterilization procedures are important.

Sweden

1. We will soon have a completely modern building and an up-to-date safety program based on good data and sound thinking.

2. We have a well-rounded safety program. We keep records of illnesses but do not list causes. Our program includes training as well as new equipment.

3. At a certain hazard level it is up to the laboratory director to stop operations and refuse to continue until proper facilities are provided. It is ridiculous to attempt 1960 research or surgical techniques with 1950 equipment and procedures and 1950 laboratory support. It is not so much that our aseptic techniques have deteriorated. We must realize that it is necessary for our techniques to be better than they were ten years ago because modern hospital surgical and research procedures demand better and safer techniques. The aim of the laboratory director should be not only to keep up with matters pertaining to safety but to keep ahead.

4. Hepatitis is the greatest laboratory hazard.

5. Procedures are or will be very close to those at the U.S. Army Biological Laboratories. Two things are needed, (a) a complete monograph on microbiological safety, and (b) adequate studies of the human factors of laboratory accidents.

6. Money for safety equipment is hard to get.

7. Safety is a part of everyone's job. Details are handled by committees. The union helps to insure that prompt action is taken.

Switzerland

1. Our laboratory is operated for profit with little regard for protection of product or personnel. It is company policy not to discuss laboratory illnesses. Our scientific staff has been unable to sell microbiological safety to management partly because they don't know exactly what to suggest or how to justify the needed changes. We need some type of safety monograph.

U.S.A.

1. The program must be run with a feeling of responsibility. The director must establish rules and insist that they be carried out. Responsibility must reach down to all levels. Training and retraining is necessary.

2. The laboratory director has a concern with safety, but he should leave policy and action to the leaders at the working level.

3. I will do anything necessary to maintain safe working conditions.

4. Everyone working with this virus will become infected.

5. All infectious operations should be carried out in ventilated work cabinets.

6. Correct approaches and techniques should be taught in undergraduate school, but an adequate summation of such teaching information is not available.

7. One must obtain a certain amount of information in order to know where to start making changes.

8. The most important rules for the laboratory are, (a) don't create bubbles in cultures, and (b) don't blow out the last drop from a pipette. Selection of workers is important. The director should try to understand the personality traits of each of his people but also should insist on absolute conformity to a few clear regulations. A course in statistics should be given to accident prone individuals. Psychological studies about the world we live in should be done on a truly scientific basis - not for an immediate applied result.

9. The principal deterrents to good safety are, (a) inadequate space, and (b) untrained technicians. In the hospital laboratory there will never be good safety so long as the foundation is all wrong. "The laboratory technician is a mercenary of the pathologist." Highly trained people have little trouble with laboratory illnesses. In a laboratory there should be unqualified enforcement of regulations.

10. Because of the many responsibilities and limited funds it is not always possible to teach good techniques to students. They can learn this later if they do infectious work.

11. Laboratory safety is much like flying a plane - most accidents are caused by pilot error. Correct technique will take care of all but a few laboratory infections.

12. Too much fuss has been made about biological hazards in laboratories. People will not face up to the price of playing marbles. After all, a foot soldier should expect to be hit with a bullet! Besides, American safety equipment is too complex. Inventors seem afraid to design things which are low cost, simple, and functional.

13. One has to separate those safety procedures which are only window dressing from those that are really needed. But here there is a serious lack of communications; one reason being that infections and events leading to infections are covered up to avoid bad publicity. The informal organization does most of the good safety work, but the real safety policy in most medical schools is to work until you are in trouble, then stop and let things cool off or call for outside help. Very often the easiest out for the Dean is to outlaw certain agents.

14. Control is simple. Provide necessary equipment and regulations - then have absolute conformity and clobber anyone who does not conform.

15. Vaccination is the most important precaution.

16. Selection of the correct disinfectants is important.

17. Control of air-borne contamination is important.

18. Some window dressing is necessary, but each laboratory should have its own rules which are followed exactly. Particular attention should be paid to aerosol-producing manipulations.

19. Prompt reporting and subsequent treatment of accidents are important.

20. Our procedures are an example of what not to do. Information on safety is so spread out I wouldn't know where to start looking for it. There is little we can do without the proper funds.

21. We cannot work on Coccidioidas immitis because the Dean has outlawed its use in the medical school.

22. We know what we should do, but we have not been able to get the money for safety cabinets.

23. A good safety program should include:

    (a) Basic training in good techniques.

    (b) Selection of workers who constantly have good technique and who have a desire for exactness of work.

    (c) All procedures must be specified.

    (d) Absolute enforcement is necessary.

24. People should have learned about laboratory safety in undergraduate school. The laboratory director should establish a strict set of regulations and deal harshly with those who do not follow them.

D. RULES AND REGULATIONS

Modern concepts of safety usually require that management initiate suitable regulations which specify the manner in which the work is to be carried out. Regulations are no less appropriate for the infectious disease laboratory than in any other work situation. In several countries (England, Sweden, and U.S.) publications in scientific journals had appeared which listed some regulations which should be followed during laboratory procedures. Some scientists in these countries have accepted these as working standards for their own laboratories. Unfortunately, these publications, for the most part, are inadequate when applied to any one particular situation and fall short of what would normally be considered an adequate set of operational safety regulations. Most countries had general standards which applied to hygenic conditions, etc., but again these were of limited value in reducing infectious laboratory risks.

Few of the laboratories visited had specific rules or regulations for microbiological safety. Those who had regulations were generally laboratories employing a relatively large number of people. It was not surprising that laboratories which had active and directed safety programs were also

those at which written laboratory safety regulations had been prepared. A total of 29 laboratories had written safety regulations while eight laboratories had regulations which had not been committed to writing. In 26 per cent of the laboratories an unwritten regulation of sorts existed since, in these laboratories, work with certain infectious agents or procedures had been "outlawed" because of the infectious risk. It would seem that all too often problems of occupational infection were solved merely by stopping all research with certain agents.

Although the laboratories as a group were inadequate in having neglected to specify procedures for the protection of personnel, in my opinion this can be in part accounted for by a lack of understanding of modern means of protecting laboratory workers and inadequate communications in this area. A majority of the laboratories were eager to receive any regulatory information which could be made available. At least 12 directors at educational institutions stated that they would like to utilize those general laboratory regulations developed by the U.S. Army Biological Laboratories as teaching aids in their bacteriology courses. In three countries, Canada, England, and Australia, individual scientists were engaged in projects in which some current information on laboratory hazards was being summarized for use in the preparation of laboratory safety regulations.

In West Germany a number of government regulations specified protective equipment and procedures that should be used in handling infectious microorganisms. One booklet, Accident Prevention Regulations for Medical Laboratories,[25] published in 1956, applies to all medical, dental, and veterinary laboratories in West Germany, even if infectious agents are not used. The regulations are augmented and further detailed by other State publications. Although not all-inclusive, these "compulsory" regulations cover many important aspects of laboratory work where physical, chemical or biological hazards may be prevalent. They do not, however, cover immunization of personnel and the reporting and investigation of accidents, injuries, and infections. Some of the pertinent regulations in this publication are summarized below:

1. All laboratories using infectious material must notify the professional association.

2. The responsible supervisor must have sufficient knowledge in the field of prevention of occupational illnesses and must have his safety duties delegated to a competent individual when he cannot be reached.

3. Laboratory personnel must be told of the hazards and the preventive measures and be constantly supervised.

4. Requirements for laboratory rooms are listed which include leakproof floors, and walls, and doors which can be washed and disinfected.

5. All mouth pipetting is prohibited. The regulation states that this rule is to be enforced within a period of three years.

6. All specimen material will be considered infectious and packaged and opened accordingly.

7. "Protective boxes" with leakproof surfaces should be used for infectious operations where aerosolization or splashing of material can occur.

8. The head must be covered when working with infectious materials.

9. Food, drinks, tobacco, and chewing gum are not permitted in the laboratory.

10. First-aid kits and persons trained in first-aid techniques must be present in each laboratory.

Unfortunately, the regulations do not specify which operations are to be carried out in "protective boxes" nor do they require that the boxes be ventilated. Change rooms are not mentioned. In the German laboratories visited these regulations were largely unknown or ignored. Regulations pertaining to "protective boxes" and to mouth pipetting were commonly disregarded.

In Sweden a list of procedural rules for handling tubercle bacilli has been published and distributed. I was told, however, that these regulations were inadequate and that most laboratories were doing far more than required in the publication.

A number of universities and commercial laboratories in the U.S. have prepared safety regulations or safety manuals. Few smaller laboratories in the U.S. and abroad have such regulations but many have written procedures for certain operations which include safety instructions. In Ontario the Public Health Department is presently preparing a Safety Handbook. At the Pasteur Institute, the Virus Department has a short list of rules pertaining to safety.

It is concluded that most people employed in infectious disease laboratories do not have detailed and written safety regulations available to them. In my opinion, most do not object to, but in fact would welcome such regulations if they are reasonable and if the rules are presented clearly and in sufficient detail. Many workers, in reading general regulations, express a desire for more details; What disinfectant and in what concentration?, What type of respirator?, What type of pipettor?, etc.

E. LABORATORY SAFETY COMMITTEES

In industrial safety programs, safety committees are frequently used as a mechanism for maintaining interest in accident prevention and for discovering and analysing hazardous situations. But committees are not necessarily used in every good safety program. This statement also appears to hold for microbiological safety programs. It is of interest nevertheless to review the frequency and types of safety committees in the infectious disease laboratories.

No laboratories with fewer than 25 employees had safety committees. Of the 65 laboratories having 26 or more employees, 21 had some type of laboratory safety committee. Thus 21 per cent of all laboratories and 32 per cent of those laboratories with more than 25 employees had safety committees. The U.S., Sweden, The Netherlands, Canada, and England were the only countries where committees were observed. The nature and functions of the committees varied widely. In the U.S. they were frequently found where there were full- or part-time safety inspectors. In the English-speaking countries laboratory technicians served as committee members more often than in other countries. Frequently the safety committee consisted of the director and several or all of his staff. Twelve of the 21 committees met at regularly scheduled intervals; eight met only when some need arose. All but two of the committees had permanently assigned members rather than a rotating membership. Eleven customarily submitted written reports of their activities.

Opinions as to the value of safety committees varied widely. Several directors felt that committees were mainly a mechanism for diluting responsibility. Others stated that every responsible laboratory chief should devote at least a portion of each staff meeting to a discussion of safety problems, making the scientific staff the committee. But the majority of the directors displayed a decidedly negative attitude toward laboratory safety committees.

It is difficult to assess the efficiency of the committees, since their responsibilities and duties varied widely. When a full- or part-time safety officer was a member of a committee, the other members usually acted more or less in the capacity of consultants. When the committee was made up of the director and his staff, corrective action to eliminate or control hazardous situations was easier than when the committee was composed of lower-level people. The most frequent shortcomings of the committees studied were:

1. Lack of knowledge about microbiological hazards (a communication problem).

2. Failure to investigate, analyze, and record accident and illness causes systematically.

3. Lack of funds to correct hazardous conditions.

4. Failure of management to provide the proper support for committees.

F. VACCINATION OF LABORATORY PERSONNEL

Vaccination of exposed personnel can be considered a part of the laboratory safety program. When efficient vaccines are available, vaccination is a good way to prevent laboratory illness. Vaccination, however, has the following general limitations:

1. Some vaccines offer only partial protection.

2. Vaccines are not available for many infectious agents.

3. Even in vaccinated persons, massive exposure can initiate an illness.

4. Laboratory techniques found to be adequate for agents for which good vaccines are used may be found to be grossly inadequate when work is initiated with another infectious agent for which personnel are not vaccinated.

In 93 per cent of the laboratories one or more vaccines were administered to exposed personnel. As a group, directors and supervisors seemed very conscientious about this activity. Of course in many instances a state or federal law required vaccination of laboratory workers against certain diseases. BCG vaccination was given to workers in 53 laboratories. In 64 laboratories personnel were given periodic chest X rays or physical examinations.

A number of laboratory directors emphasized the need for good vaccines against viral and rickettsial diseases. Most frequently mentioned were Russian spring-summer encephalitis, B-virus and Q fever. Several directors were concerned over the use of immunizing preparations made from mouse brain tissue (e.g. the Japanese B encephalitis virus vaccine) and for that reason held the number of people being vaccinated to a minimum.

In a few laboratories the idea persists that immunity for some diseases is best achieved in laboratory workers by allowing them to be occupationally infected. In my opinion this is a dangerous policy which cannot, in the final analysis, be completely justified. The laboratory director who has a small amount of work to be done with the tularemia organism may be justified in selecting several laboratory people who have previously had the disease. But such stop-gap measures are not an adequate substitute for the use of proper safety equipment and good laboratory technique. In the brucella laboratory of one institute I was told that only persons who had had brucellosis were ever allowed to enter or work in that laboratory.

The notion that active infection is a technique for immunizing laboratory workers is frequently complamented by another spurious belief. This is that with some infectious diseases, notably Q fever and psittacosis, it is impossible to prevent laboratory infections. Failure to prevent illnesses due to these highly infectious agents is simply a reflection of the inability of the techniques and/or equipment used to contain the pathogenic microorganisms.

G. TRAINING PROGRAMS

Another inadequacy among the infectious disease laboratories was the absence of training and orientation programs. Only 14 of 102 laboratories had any type of established program for training workers in accident prevention and only ten provided safety orientation for new employees. In four instances, (one in Canada, one in England, and two in the U.S.) the training programs seemed to be comprehensive and well planned. The remaining ten programs could be classified according to activity as follows:

Presenting films on safety	- 2 (England and U.S.)
Providing reading material on safety	- 2 (England and France)
Lectures on laboratory safety	- 3 (one in England, and two in U.S.)
Apprentice method	- 3 (France, Portugal, and U.S.)

I was encouraged to note the interest shown in the microbiological safety films which have been prepared by the U.S. Army Biological Laboratories. At least 30 laboratories indicated that they wished to use the films, if available, for teaching and training purposes. Information on the availability of these films was given to all laboratory directors. In my opinion the need for special instruction and training in procedures and techniques for handling pathogenic microorganisms is becoming increasingly recognized in laboratories throughout the world and the coming decade will see a substantial increase in activities of this nature.

H. CONTRACTOR PERSONNEL

Little specific information was obtained concerning arrangements that might be made for outside contractor personnel who come into infectious disease laboratories. The defense establishments visited had their own repair and machine shops and there was little necessity for outside craftsmen to do work in infectious buildings. Likewise some large institutes such as The National Institute of Public Health in Holland and the commercial firms had maintenance and shop personnel. As far as could be determined little consideration was given in most other laboratories to hazards that might be created when outside workmen were required to work in infectious disease areas. In fact, in several laboratories, renovation procedures by outside workmen were in progress in infectious areas while the laboratory operations continued.

Management at the National Institute for Medical Research in London has, however, recognized the problem and has established a policy to be followed. When it is necessary for outside contractor personnel to work in infectious laboratories, the area is first decontaminated, usually with formaldehyde. The probable hazards and the decontamination precautions are explained to the contractor. If necessary, the institute provides skin tests and X-rays of the workmen. However, no agreement is made that the institute will pay the medical expenses of anyone who becomes occupationally ill.

V. LABORATORY BUILDING DESIGN

The facilities provided for infectious laboratories have an important relationship to microbiological safety. Good design features for buildings and rooms can be valuable in containing and controlling infectious agents. If a building is not properly designed, its features can complicate or limit efforts to minimize risks of infection and cross contamination. Those instances of laboratory epidemics cited in Chapter III are examples of how air-borne contaminants may spread from one room to other areas throughout the building. Almost all the design features of a laboratory building may be said to affect microbiological safety to some degree, but among the most important are:

1. Size and shape of the building.
2. Room size and layout arrangements.
3. Methods for heating and ventilating.
4. Use of air locks and other means of separating infectious areas.
5. Methods of treating contaminated air.
6. Treatment of sewage.

This chapter describes many of the design features of the laboratories studied which are significant in assessing the status of microbiological safety.

A. ARCHITECTURAL TYPES

The institutes studied reflected the diversity of architectural designs throughout the last 90 years. Ornate, castle-like structures built at the turn of the century were in sharp contrast to the clean, functional, or ultramodernistic designs of buildings completed in recent years. Not in such sharp contrast were the actual laboratory rooms provided in the older as compared with the more recently built structures. In many of the modern structures the decorative color schemes, lighting, and lower ceilings of the laboratory rooms were the only essential differences between laboratory rooms in older buildings. Indeed, some of the older structures which had been extensively renovated provided better safety features than some new buildings.

Figures 4 through 9 are selected examples of a few of the laboratory buildings. Figures 4 and 5 show some of the structures inspected which are 40 or more years old. Figures 6 and 7 depict semimodern buildings built between 10 and 30 years ago. The buildings shown in Figures 8 and 9 are examples of structures completed within the last ten years.

B. AGE DISTRIBUTION OF LABORATORY BUILDINGS

The dates of construction of 82 foreign and U.S. laboratory buildings are summarized in Table XXVI. More than one half were less than ten years old. Of the 43 laboratories in this category, 36 were less than five years old and 19 had been occupied within the last three years. Buildings under construction at the time of my visit are not included in Table XXVI. Although about 10 per cent of the buildings were greater than 50 years old (the oldest was built 90 years ago), many have been extensively renovated. In the table, influence of the two world wars on laboratory building construction is evident.

TABLE XXVI. AGE DISTRIBUTION OF 82 U.S. AND FOREIGN LABORATORY BUILDINGS

AGE IN YEARS	PER CENT		
	U.S. Laboratories	Foreign Laboratories	U.S. and Foreign Laboratories
Less than 10	61.5	50.7	52.4
11 to 20	0	5.8	4.9
21 to 30	15.4	18.8	18.3
31 to 40	0	7.3	6.1
41 to 50	15.4	7.3	8.5
51 or greater	7.7	10.1	9.8

C. SPACE RELATIONSHIPS IN LABORATORIES

Several laboratory directors suggested that inadequate per capita space within laboratories might be responsible for increased risks. To test this hypothesis an analysis was made of the amount of space available to persons in 32 laboratories in 15 countries. In more than half the laboratories, 100 to 500 square feet of building area per employee were available (Table XXVII). The average per capita space was 608 square feet. Only six per cent of the laboratories had less than 100 square feet per person. In 14 laboratories, where students were also accommodated during part of the year, there was an average of 728 square feet per employee (not counting students); 86 per cent of the workers had between 200 and 1000 square feet of building area (Table XXVIII). These figures compare favorably with unpublished calculations of infectious disease laboratories at the U.S. Army Biological Laboratories, where the per capita space available varied from 200 to 1100 square feet, with an average of 600 square feet per person.

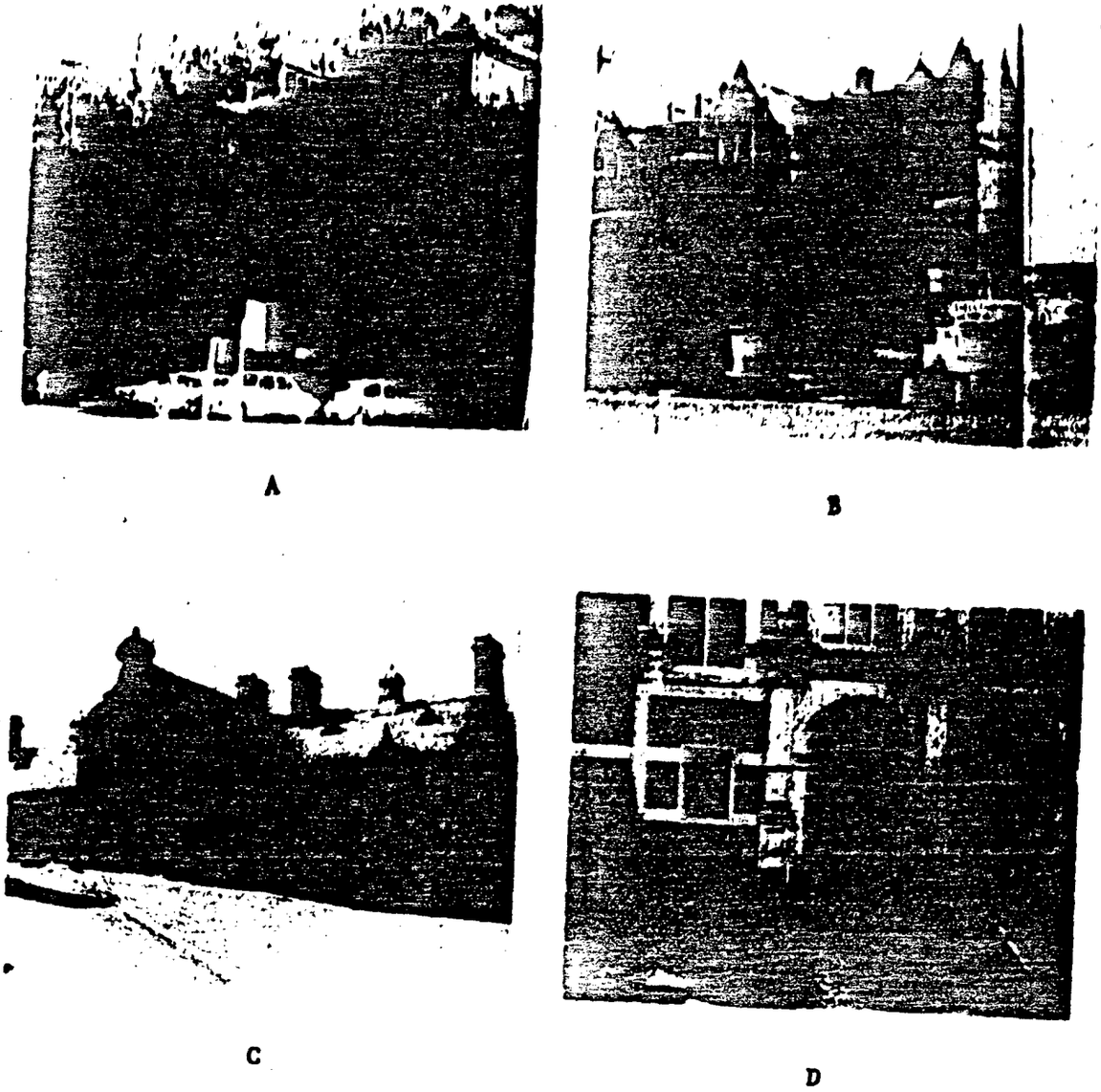

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Figure 4. Older Laboratory Buildings.
A. The George William Hooper Foundation, University of California Medical Center, San Francisco, California.
B. The Lister Institute of Preventive Medicine, London, England.
C. Virus Reference Laboratory, University of Glasgow, Ruchill Infectious Disease Hospital, Glasgow, Scotland.
D. The Robert Koch Institute, West Berlin, Germany.

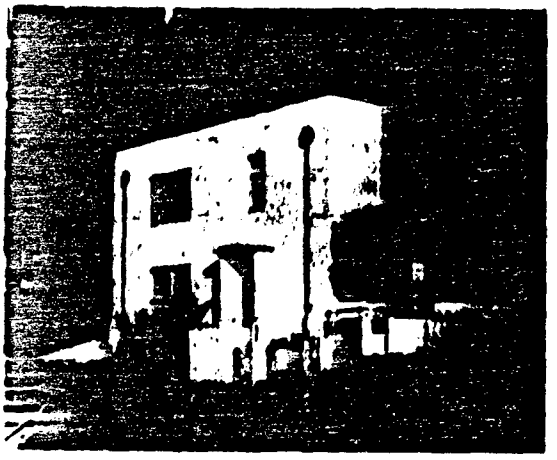
A

B

C

D

Figure 5. Older Laboratory Buildings.
A. Paul Ehrlich Institute, State Institute for Experimental Therapy, Frankfurt am Main, Germany.
B. The Bernhard Nocht Institute for Naval and Tropical Diseases, Hamburg, Germany.
C. Institute of Hygiene, Norwegian Veterinary College, Oslo, Norway.
D. Department of Bacteriology, University of Lund Medical School, Lund, Sweden.



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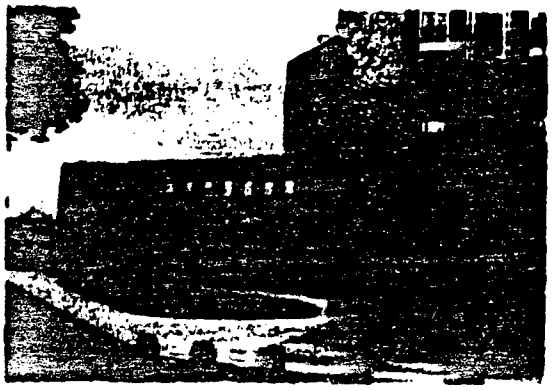

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Figure 6. Semi-Modern Laboratory Buildings.
A. Plague Building, University of California Medical Center, San Francisco, California.
B. Henry Phipps Institute, University of Pennsylvania, Philadelphia, Pennsylvania.
C. The National Institute for Medical Research, Mill Hill, London, England.
D. London School of Hygiene and Tropical Medicine, University of London, London, England.

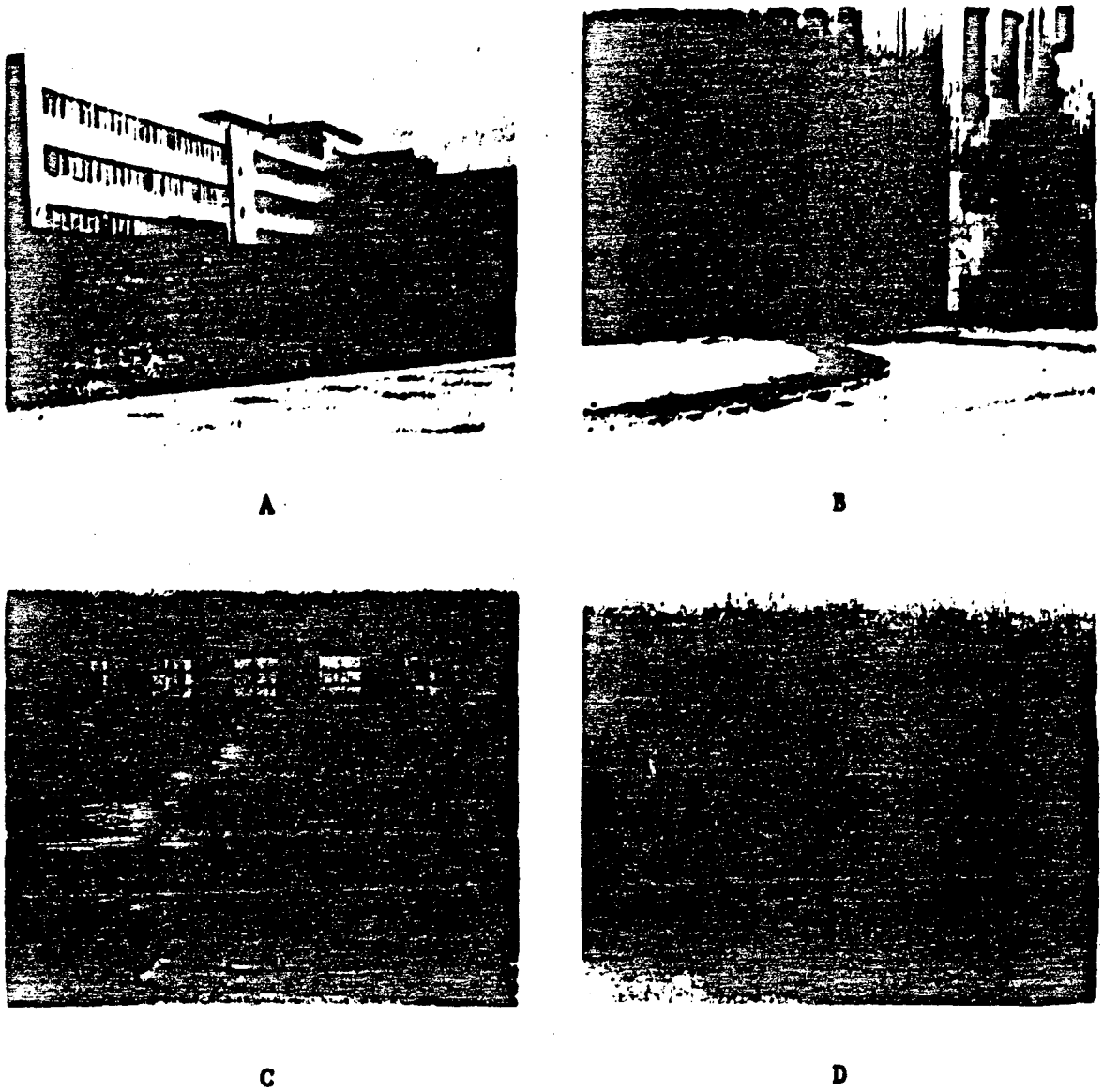

Figure 7. Semi-Modern Laboratory Buildings.
A. Department of Bacteriology, University of Aberdeen, Aberdeen, Scotland.
B. Institute of Hygiene and Microbiology, Medical Faculty, University of Dusseldorf, Dusseldorf, Germany.
C. Institute of Bacteriology, University of Uppsala, Uppsala, Sweden.
D. Bacteriological Institute, Medical School, University of Gothenburg, Gothenburg, Sweden.

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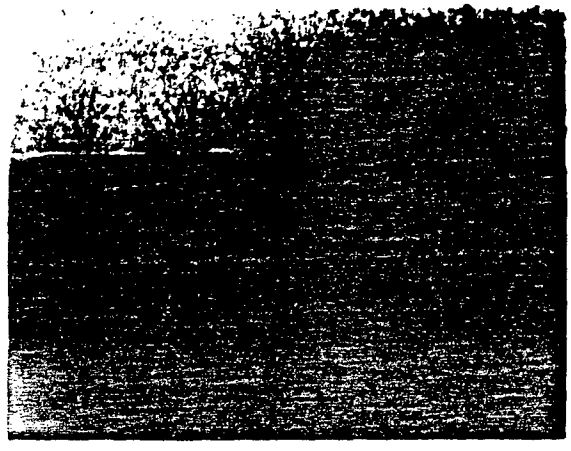

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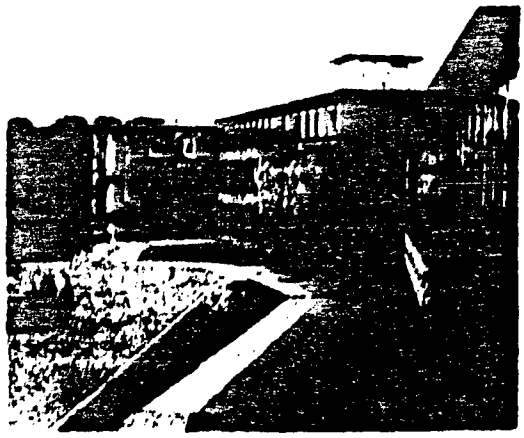
Figure 8. Newer Laboratory Buildings.
A. Wisconsin State Laboratory of Hygiene, Madison, Wisconsin.
B. Department of Infectious Disease, University of California Medical School, Los Angeles, California.
C. Life Sciences Building, Southern Illinois University, Carbondale, Illinois.



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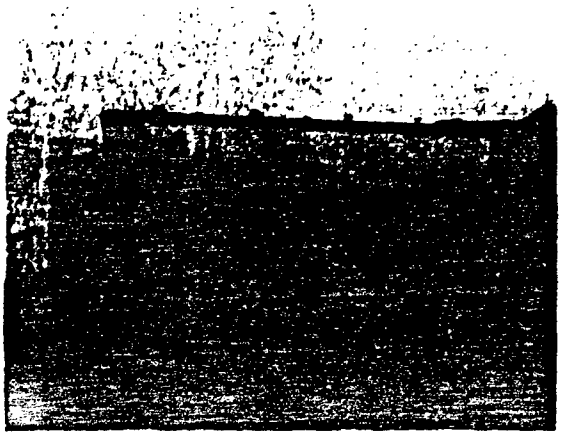

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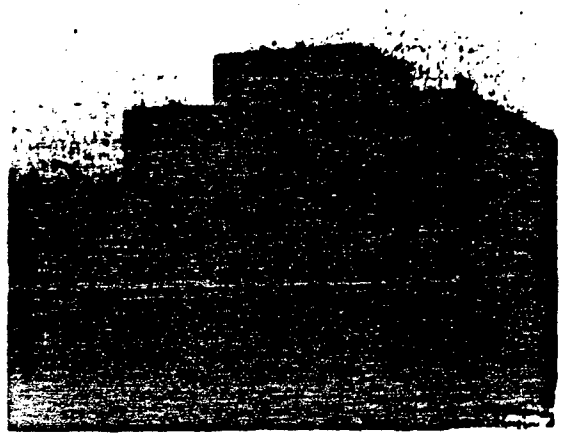

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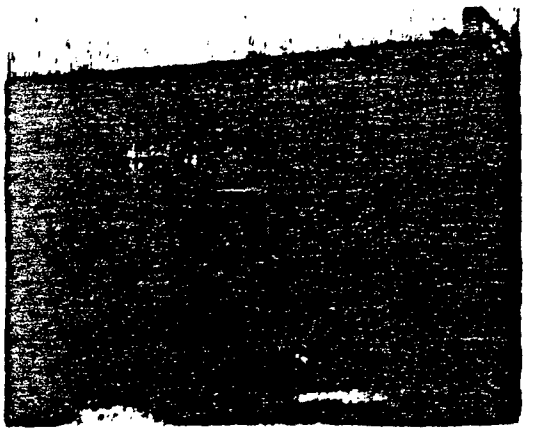
D. Research Laboratories, Pharmaceuticals Division, Imperial Chemical Industries Limited, Macclesfield, England.
E. Animal House, Imperial Chemical Industries Limited, Macclesfield, England.
F. Research Division, Glaxo Laboratories Limited, London, England.



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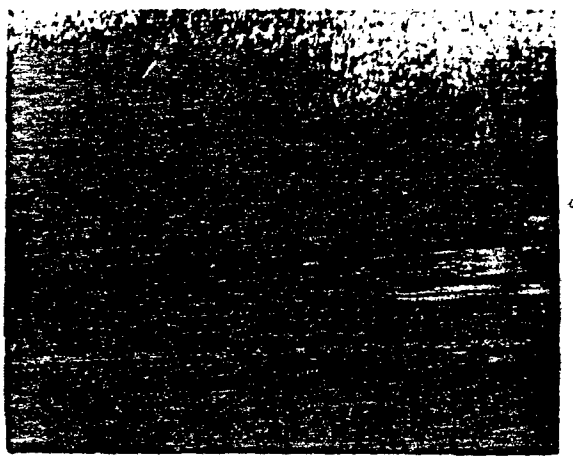

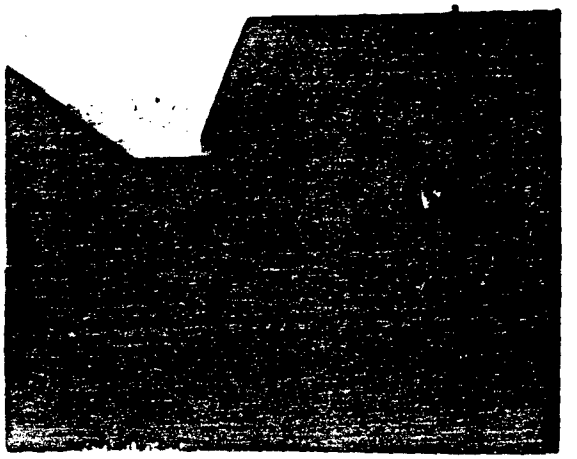

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Figure 9. Newer Laboratory Buildings.
A. State Bacteriological and Public Health Institution, Munich, Germany.
B. Virus Laboratory, Statens Seruminstitut, Copenhagen, Denmark.
C. Department of Bacteriology, Karolinska Institute, Stockholm, Sweden.

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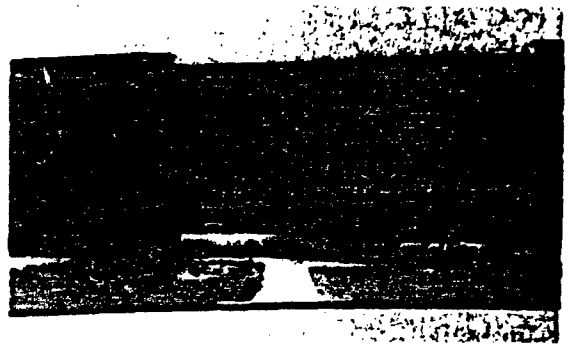

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D. Institute of Bacteriology, University of Oslo, Oslo, Norway.
E. Institute of Tropical Medicine, Lisbon, Portugal.
F. The John Curtin School of Medical Research, The Australian National University, Canberra, Australia.

TABLE XXVII. SPACE RELATIONSHIPS IN 32 MICROBIOLOGICAL LABORATORIES

FLOOR AREA, Sq Ft Per Person	PER CENT
less than 100	6
101 to 500	53
501 to 1000	28
1001 to 2000	13

Average floor area per person - 608 sq ft

TABLE XXVIII. SPACE RELATIONSHIPS IN 14 LABORATORY BUILDINGS IN WHICH STUDENTS WERE ALSO ACCOMMODATED*

FLOOR AREA, Sq Ft Per Person	PER CENT
200 to 500	43
501 to 1000	43
1001 to 2000	14

Average floor area per person - 728 sq ft

* Note: Students not included in calculations.

While crowding may be a hazard-producing problem in some infectious disease laboratories, it does not seem to be a general problem when measured on a space available basis. Factors more important in assessing microbiological hazards would be (a) efficiency of space utilization, and (b) laboratory designs and furnishings.

D. NEW LABORATORY CONSTRUCTION

At 54 per cent of the institutes included in the study a new building had been recently occupied (within one year), was presently under construction, or was in the "blueprint" stage. Four buildings were under construction at the time of my visit; 26 were in the planning stage. Of 45 present or future structures on which specific information could be gathered, only 11 could be classified as having adequate safety facilities. Twelve laboratories had moderate but insufficient safety facilities. But in 22 existing or planned new buildings little or no safety provisions were included.

Specific features included in the new or planned buildings are as follows:

1. 51 per cent of the new buildings had or will have air filtration systems, although most of the systems were for the filtration of supply air.

2. 56 per cent had or planned to have cabinets in the infectious disease laboratories, although in many instances the cabinets were not ventilated or were in other ways inadequate.

3. 42 per cent had or planned to have some type of change room for laboratory personnel. Many did not include shower facilities and others were not located so as to separate clean and infectious areas.

4. 42 per cent had or planned to have ultraviolet air locks.

5. 18 per cent had or planned to have systems to treat potentially contaminated sewage. With one exception these were for the treatment of effluents from poliomyelitis vaccine production or testing laboratories. All were heat treatment systems in which collected fluids were treated with steam in batch manner, usually at a temperature of 80° to 90°C for one to two hours.

E. COSTS OF LABORATORY CONSTRUCTION

Data on the cost of recently completed laboratories, or laboratories presently under construction, in six countries are shown in Table XXIX. While it is difficult to avoid equivocation in the use of these estimates since no correction is made for the relative purchasing power of foreign money, a considerable variation in the cost of new building construction is indication. For example, the cost per square foot for nonequipped laboratory buildings, among those for which data were available, varied from a low of $14.00 in Finland to a high of $50.00 in one Swedish laboratory. Likewise, when the cost of equipment is included, a new laboratory in Norway cost $23.00 per square foot while a Swedish laboratory gave an estimate of $70.00 per square foot.

Of those laboratories referred to in Table XXIX only the two being constructed in Sweden were considered completely adequate for infectious disease work. For comparison, cost estimates of a recently renovated Norwegian tuberculosis laboratory suite and a newly completed English facility for rearing specific-pathogen-free animals is included.

These data serve to illustrate a problem facing many laboratory directors. How can the director convince his administrative peers that the cost of constructing and equipping a satisfactory and modern infectious disease

laboratory is much higher than the cost of other government, municipal, or educational structures? Even if it were administratively allowed, most directors, in planning a new facility, will hesitate to reduce the size of the planned structure in order to allow a greater expenditure per square foot of space. They frequently find themselves without sufficient information on laboratory hazards, on the frequency of laboratory illness, or about recent developments in building design — information which is needed to present cogent arguments for increased building funds. Swedish scientists have been eminently successful in this area.

TABLE XXIX. COST DATA ON NEW LABORATORY BUILDINGS IN SIX COUNTRIES

COUNTRY	SQ FT OF FLOOR AREA	COST PER SQUARE FOOT WITHOUT EQUIPMENT	COST PER SQUARE FOOT WITH EQUIPMENT
U.S.	28,000	$26	$53
Australia[a]	150,000	21	--
Finland	120,000	14	--
Sweden	45,000	44	55
Sweden	40,000	50	70
England	75,000	28	--
England[b]	18,000	--	85
Norway	37,450	20	23
Norway[c]	2,500	--	14

a. Only a small portion of this building will be devoted to microbiological laboratories.
b. Facility for raising specific-pathogen-free animals.
c. Renovating and equipping an existing laboratory for TB work.

F. BUILDING DESIGN FEATURES

Discussion and illustration of some layout arrangements for buildings and suites of rooms used with infectious agents are presented in this section. These are by no means typical of most laboratories studied but, rather, represent some of the laboratories in which an attempt had been made to improve containment of hazardous microorganisms through building design. Not illustrated in this section are a number of recently designed buildings — some completed and some under construction — which contained no design features for isolation of infectious areas. Although modern colors and shapes provide a pleasing initial appearance, room arrangement and laboratory layout in new structures were often little different from that found in older laboratory buildings.

1. A U.S. Virus Laboratory Suite

An infectious disease unit located in a U.S. teaching institution is shown in Figure 10. Located at the end of one floor of the building, the four-room suite is isolated from other laboratories by an ultraviolet air lock. The isolation area is maintained at a lower air pressure than the remainder of the building. Exhaust air is passed through "absolute type" filters. The change room is suitable only for the changing of coats and shoes; no shower is provided. Manifold piping and a separate air filter system for ventilated cages is provided in the animal room.

While this design allowed good isolation for infectious operations, some of the errors subsequently discovered by the laboratory director illustrate a difficulty also encountered in several other laboratories. This relates to inadequate communication between the laboratory director, who generally has a strong voice in the design of a new building, and the architects and engineers. It emphasizes also the importance of adequately prepared design criteria to assist both parties in considering all aspects of a design which are needed to provide the desired degree of isolation. The mistakes uncovered in the design of this suite are as follows:

a. The cabinet is connected to the room air exhaust system and has no mechanical blower, consequently, an inadequate amount of air is drawn into the cabinet.

b. To maintain the correct air balance, the absolute filters must be changed every two to three months. This has become prohibitedly expensive.

c. The supply air for the suite comes from a common supply system. This creates a possibility for retrograde contamination to clean areas of the building.

d. Vertical pipe chases on the outside walls of the building are not sealed between floors, presenting a second opportunity for contamination of clean areas.

e. Interconnections between infectious and clean areas through the space above the false ceilings also provide means of cross-contamination.

2. U.S. Tuberculosis Research Laboratory

Figure 11 shows the room arrangement in an isolation unit of a laboratory where aerobiological experiments with tubercle bacilli are carried out. The unit was built in the basement of an existing building. Clean and contaminated locker rooms are provided, although no shower is available. Infected, aerosol-exposed animals are held in nonventilated, wire bottom cages. Animal droppings are collected on paper below the cages. When an animal cage rack is empty it is rolled in toto into the cage steamer for decontamination. All laboratory manipulations are done in two ventilated cabinets. Ceiling mounted ultraviolet lamps are provided in all rooms.

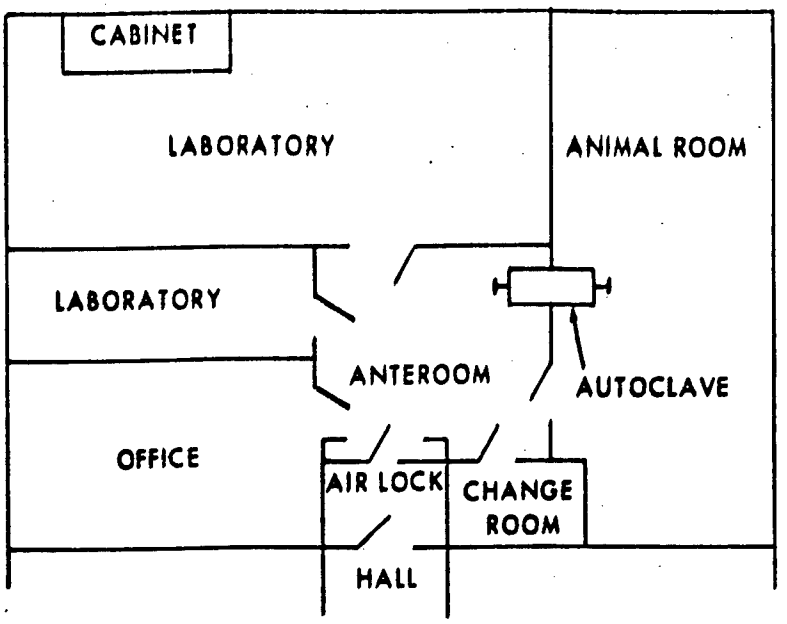


Figure 10. A U.S. Virus Laboratory Suite.

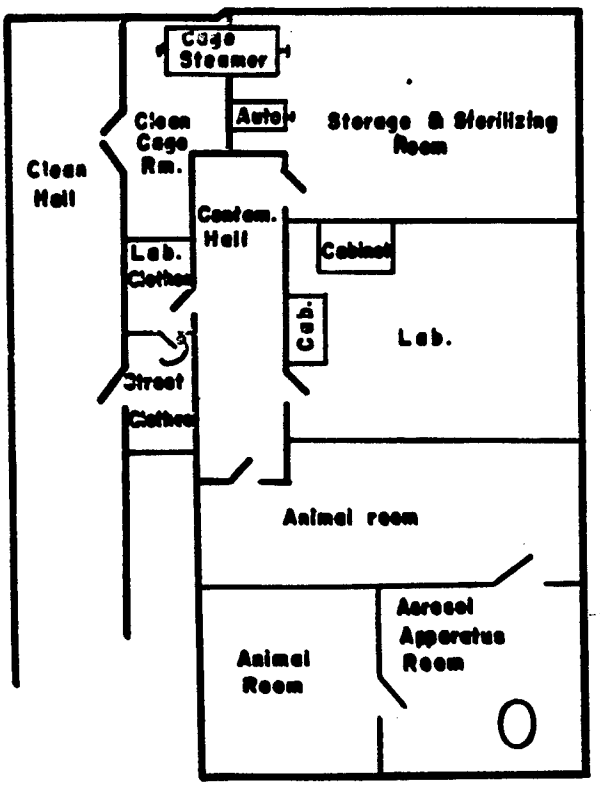


Figure 11. A U.S. Tuberculosis Research Laboratory.

3. A U.S. Pathogen-Free Animal Isolation Area

A facility for rearing or holding specific-pathogen-free (SPF) animals developed by Graham and Feenstra[26] is shown in Figure 12. This design embodies some basic features that should be considered in animal isolation areas where the problem is to safeguard the animal from accidental or unintentional infection. Isolation facilities of this type will undoubtedly find wider use as researchers in all fields continue to realize the importance of using healthy animals free of apparent or inapparent infections. Of course, a two-directional isolation problem exists when SPF animals are to be used in infectious disease work and when protection for man also must be provided.

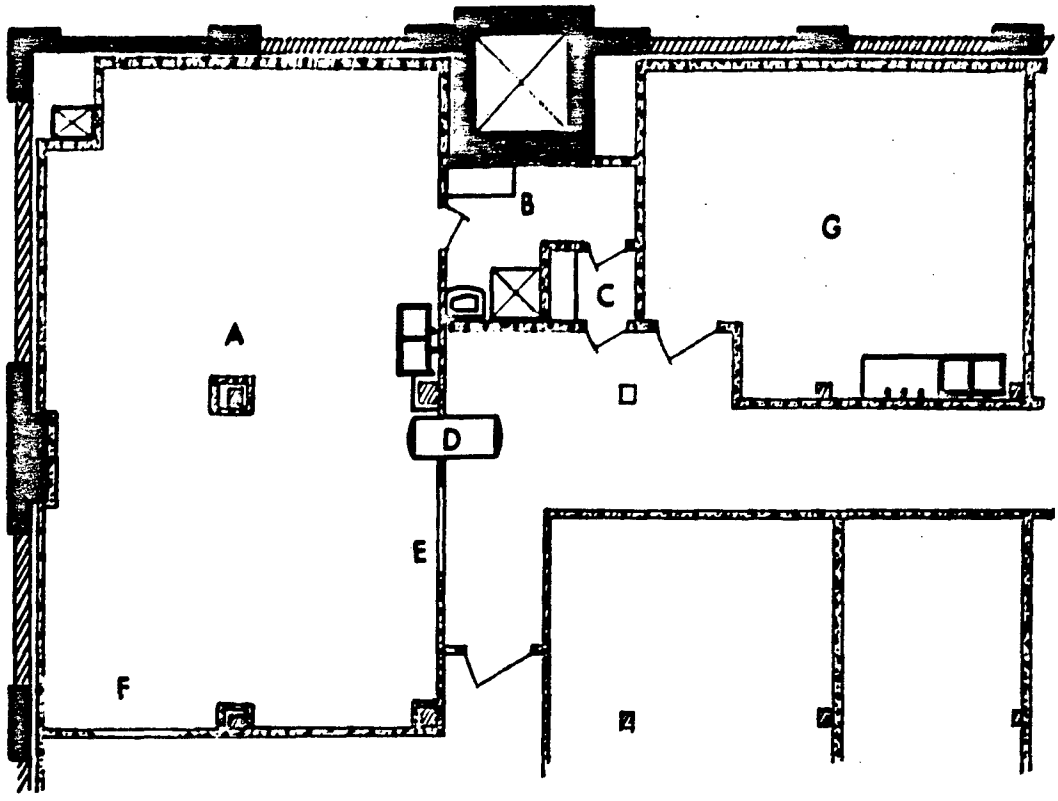
Room A in Figure 12 is an animal isolation room which is maintained under a positive air pressure. Supply air is rendered essentially sterile by a four-stage air treatment system consisting of (a) dust filtration, (b) electrostatic "filtration," (c) ultraviolet irradiation, and (d) bacterial filtration. No air is recirculated. Entrance to the room is through a double locker room system. An autoclave is provided for the sterilization of entering materials and equipment. As many of the utilities as possible are made to be serviced from outside the room. Interior wall surfaces are washable.

4. A British Poliomyelitis Vaccine Production Building

A building of unique design was completed in 1957 for the Wellcome Research Laboratories at Beckenham, Kent.[27] Shown in cross section in Figure 13, this poliomyelitis vaccine production building has a novel arrangement for providing utilities and services to laboratory rooms.

The three-story brick building is 157 feet long and 50 feet wide and provides a total of 25,000 square feet of floor area. It was the first of five new laboratory buildings which have been completed in a 5.6 million-dollar rehousing and expansion program. The poliomyelitis building cost approximately $700,000 or about $28.00 per square foot. Other buildings similar or larger in size which have been built using essentially the same design criteria are (a) a virus vaccine building, (b) a virus research building, (c) an anerobic bacteriology building, and (d) an immunology department building.

At each end of the poliomyelitis vaccine production building is a plant or utility room for large motors, and other equipment which extends the height of the building and connects with the utility spaces or "voids" located above and below each floor. The utility spaces are not void but contain pipes, air ducts, water and drain lines, and other utilities which serve the rooms above and below. The design is intended to reduce to a minimum the number of ducts, pipes, and other dust catching facilities which enter each laboratory room. Almost all routine maintenance and servicing can be done without entering the rooms. The half-floor utility spaces have a height at the center of the building of six feet six inches and slope to a minimum internal height of three feet at the outside wall.



LEGEND

A. The pathogen-free animal room
B. Inner locker room
C. Outer locker room
D. Autoclave
E. Observation window
F. Removable panel
G. Laboratory

Figure 12. A U.S. Pathogen-Free Animal Isolation Area.

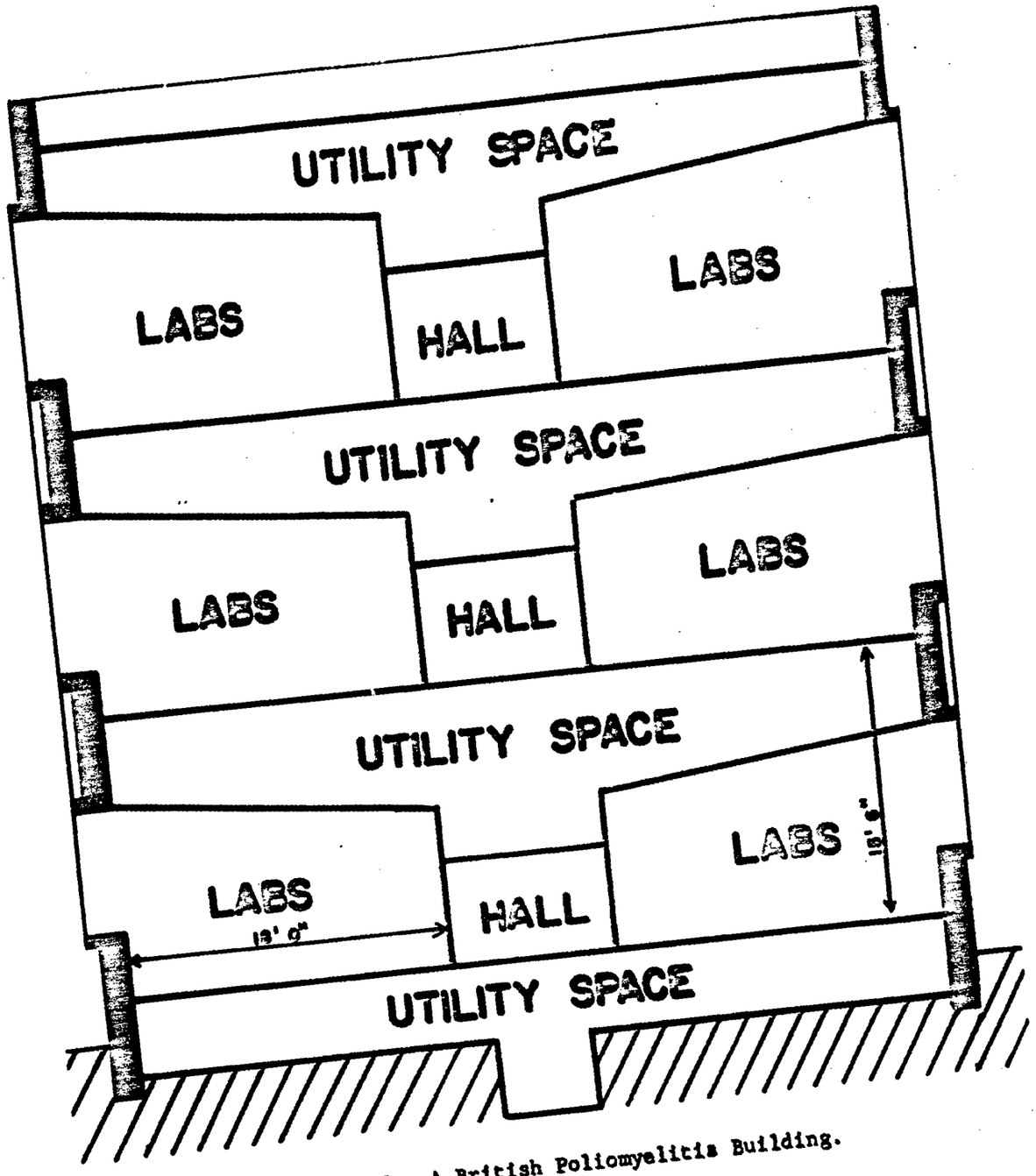


Figure 13. A British Poliomyelitis Building.

Ventilation in the building is compartmentalized; it is supplied to most rooms by small units located overhead in the utility spaces. One ventilation unit serves one or several rooms of similar function. "Sterile" areas are maintained at a positive pressure in relation to other areas. In some rooms supply air is passed through high efficiency (99.95 per cent) filters. The filter, however, must be serviced from the laboratory rooms. Heat for laboratory rooms is supplied partly in the supply air and partly from electrical heating elements encased in the ceiling of each room. I was told that this method of heating was not entirely satisfactory.

The outer wall of each laboratory includes large picture windows (non-thermopane type) with center portions which open. These are inconvenient because of the heat and glare from the sun. Large awnings have been installed on the outside of many windows.

Stairwells, elevators, and entrance doors are located at the ends of the rectangular shaped building. There are no weight bearing internal walls; the building weight is borne by vertical columns located on 13-foot centers in the corridor walls. Laboratory room furniture is designed for easy cleaning. In most rooms, tables rather than cabinets are used, and storage space is provided by wall cabinets. All table tops are of a light colored "Formica." Frequent use is made of equipment air locks in the walls between laboratories. Speaking diaphragms of a design similar to that developed by the U.S. Army Biological Laboratories are also used in walls separating certain rooms. The thin walls between rooms, which include large amounts of glass, can be easily moved.

Change rooms are provided for most areas. In some instances secondary change rooms are used as a further precaution against the spread of contamination. All facilities, however, are designed to protect the product rather than the worker. No ventilated cabinets or ultraviolet radiation are used.

5. A British Research Laboratory

Important features in the design of a series of laboratory buildings for research completed in 1957 by a British chemical firm will be discussed below.

a. Biological Laboratories

A section of the two-story biological laboratory building is shown in Figure 14 to illustrate how a basement below the first floor corridor and an attic area above the second floor corridor are used for utility and service machinery, pumps, motors, filters, and other equipment. Facilities from the basement (water, drainage, air, electricity, vacuum, and steam) rise through vertical pipe chases located along the corridor wall. A group of service outlets enters each laboratory through channels in the walls and under the floor. Air ducts running in horizontal chases

above the first and second floor corridors rise through the vertical chases to the attic where the filters and exhaust fans are located. The distilled water apparatus is located in the attic. Glass piping delivers the water to central dispensing points in each corridor. Each laboratory suite has its own air exhaust system and filters. The filters can be sterilized with formaldehyde vapor before replacement. Air is delivered to the rooms from a central system.

Large windows on the outer walls have two panes of glass spaced about 18 inches apart. Steam pipes in this space prevent moisture condensation. Venetian blinds between the glass panels can be operated from the rooms. The outer glass panels can be opened for cleaning.

Figure 15 shows one basic arrangement of a suite of rooms which has unusual flexibility. The room arrangement can be changed to accommodate pharmocological, parasitological, or microbiological research. The suite consists of a central area containing an office and utility area with a standard size laboratory on each side. No furniture is fixed. Tables, cabinets, and other equipment and furniture can be moved from place to place or returned to the stock room. A pedestal unit containing a sink and service outlet can be "plugged in" at a variety of locations by removing a floor partition and connecting to the services below. In the utility section of the center room two ventilated hoods are permanently installed, but the remaining area can be arranged in a variety of ways by the use of lightweight wall partitions which attach by lugs in the ceiling. In Figure 15 these walls have been placed so as to form a dark cubicle for microscopic work and two sterile cubicles which are entered through an air lock. Each sterile cubicle can be provided with a portable, all-metal, ventilated cabinet which can be plugged into a ceiling outlet which provides the exhaust. A number of small air outlet ducts in the ceiling of this area assures ventilation in any sized cubicle formed by the movable walls.

b. Animal House

A cross section of the two-story animal house adjoining the laboratory building is shown in Figure 16. All rooms open only to an outside, screened veranda. Each room is color coded; red and blue areas are for animals infected with microorganisms dangerous to man and white areas are for animals in quarantine or being used for noninfectious metabolic or toxicity studies. All services originate in the attic and reach the rooms via vertical chases on the outside walls. The non-recirculating ventilation system provides a minimum of ten changes of air per hour in each room. Figure 16 shows two low-hazard virus animal rooms on the lower floor and rooms with ventilated cages and autopsy cabinets for tuberculosis infected animals on the second floor. (See pages 210 and 215 for descriptions of those items.)

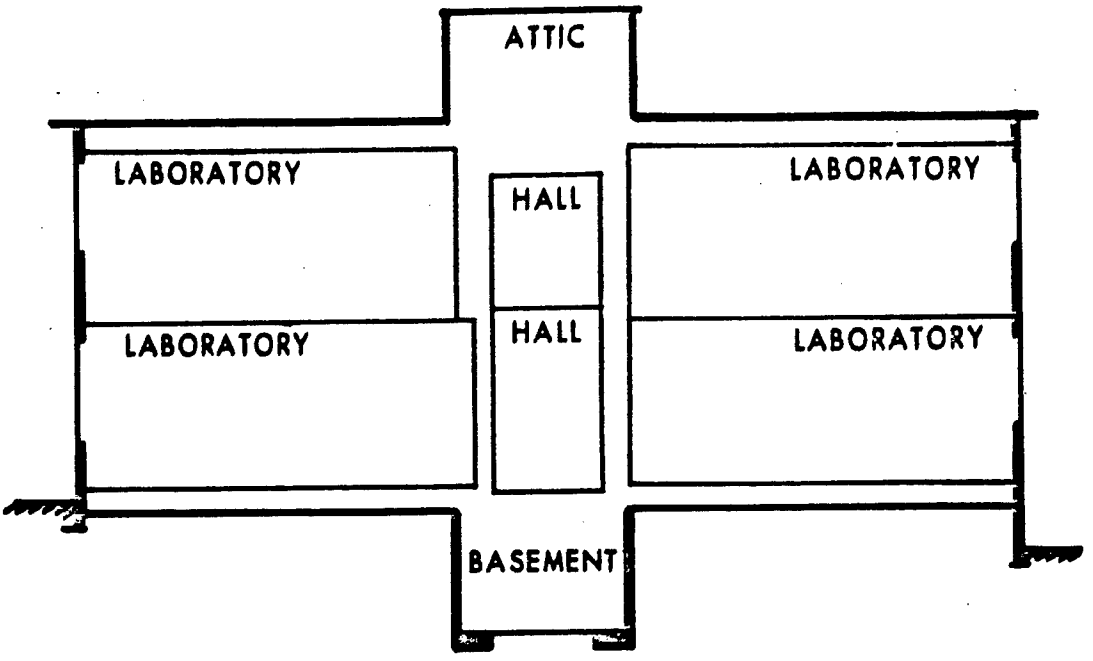
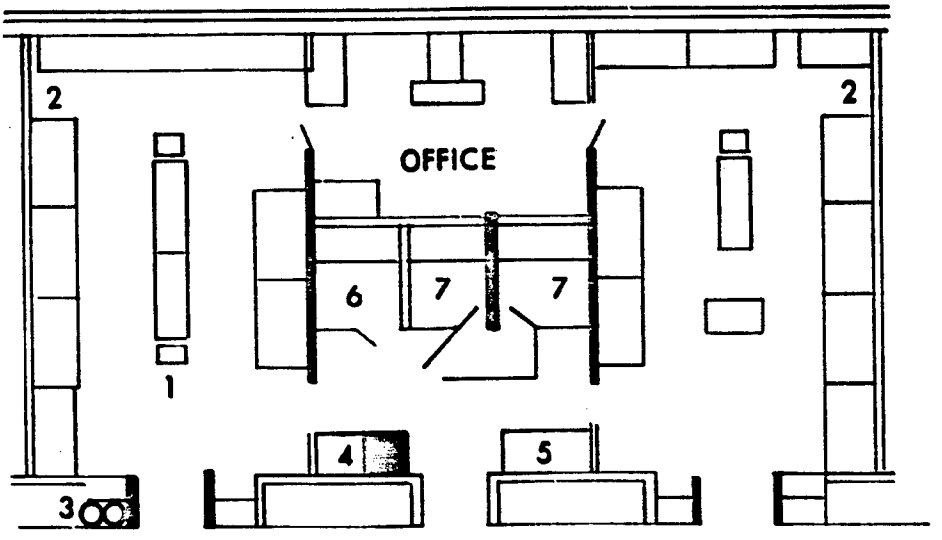


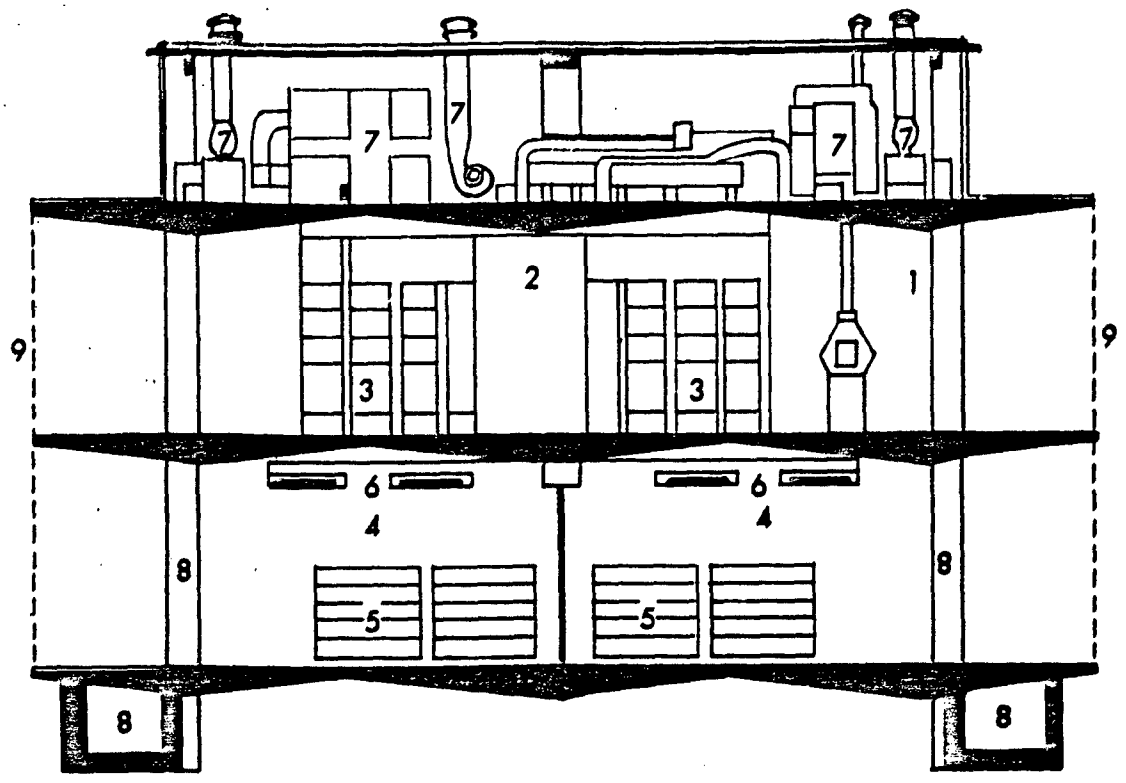
Figure 14. Cross Section of a British Biological Laboratory Building Showing Utility Spaces.



LEGEND

1. Pedestal unit
2. Standard service units
3. Cylinder gases cupboard
4. Centrifuge hood
5. Ventilated hood with UV
6. Dark cubicle
7. Sterile cubicles

Figure 15. Laboratory Suite in a British Laboratory Building.



LEGEND

1. P.M. and Culture room
2. Manipulation hood
3. Ventilated animal cupboard
4. Virus animal room
5. Movable animal racks
6. Low-velocity air diffusers
7. Extractor fans and filters
8. Services
9. Bird screens

Figure 16. Cross Section of a British Infectious Animal Building.

Figure 17 shows the floor plan of the second-floor rooms shown in cross section in Figure 16. This is one of two "isolation areas" in this building. In each, two animal holding rooms, each with an adjoining post-mortem room, are separated by a sterilizing area which connects, via an autoclave, to a cage washing room. Change rooms for animal attendants are provided in an adjoining building.

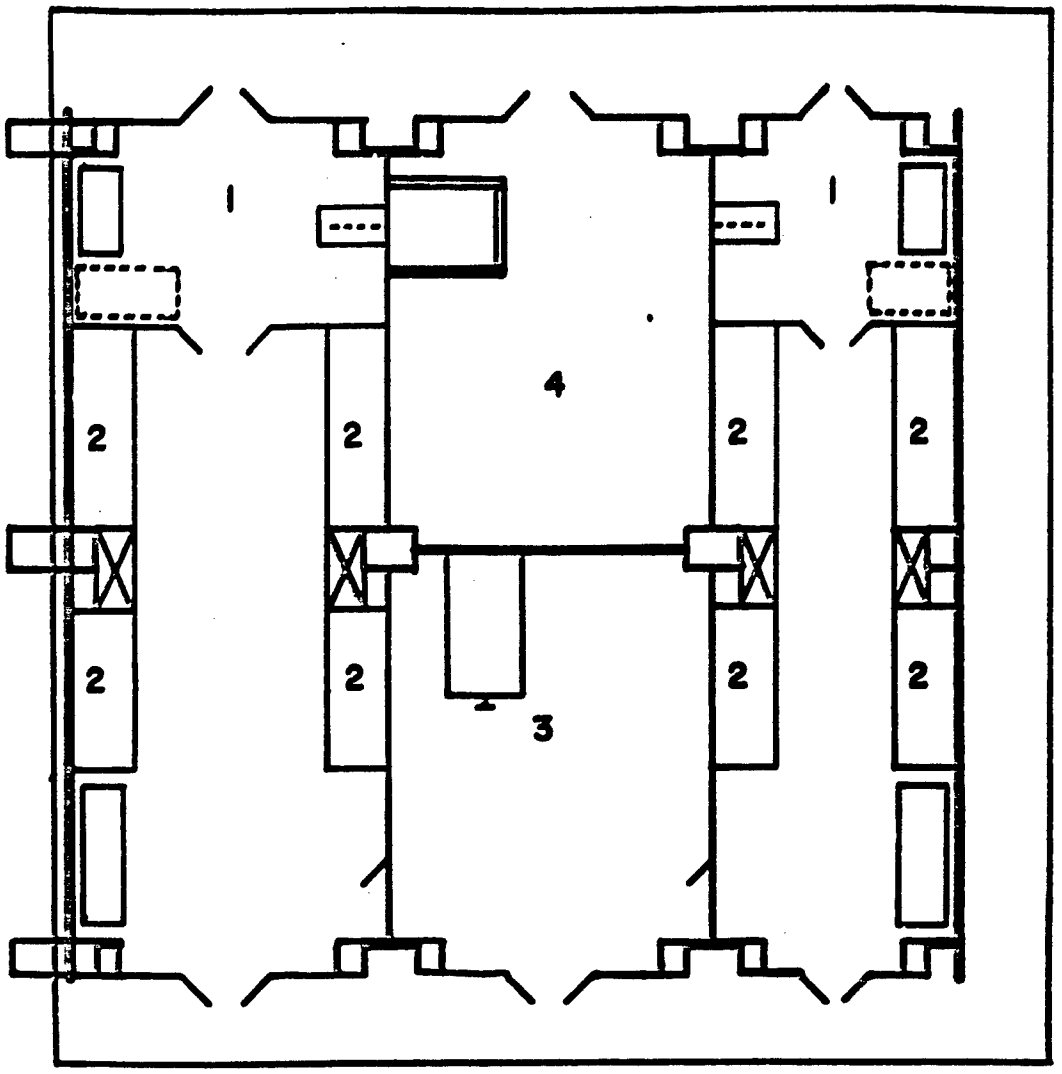
6. An Animal House in England

Figure 18 is a floor plan of a house for infected animals built in an existing structure at the Lister Institute in London.[28] One of a complex of five animal buildings, this structure has several features in common with another animal house to be described, but lacks change room facilities and a central ventilation system. A drainage gully in the floor along the outside wall of each animal room is kept half filled with a disinfectant solution. Water collecting in the gully is allowed to mix with the disinfectant and is then drained by a foot operated device which removes or replaces a stopper in the drain line. Shelves for animal cages hang from the ceiling. The rooms are separately ventilated by extractor fans which provide four to six changes of air per hour.

7. An Animal House in Scotland

The animal house illustrated in Figure 19 was designed by Grist[29] at the University of Glasgow to provide isolation of clean and virus infected animals. It is not intended to provide protection against the more highly infectious viral agents. The house was built behind an existing laboratory building and connected to the building by a covered patio which is used for cleaning and storing cages. The clean and infectious areas are, in fact, two separate buildings, each with a separate ventilation system. Ventilation rates for the infectious building are seven air changes per hour for the corridors and nine changes per hour for the rooms. Air from the infectious area is discharged unfiltered at the top of the adjacent four-story building. Infectious animal rooms are maintained at a slightly reduced air pressure. The clean building is equipped with a radiator heating system and ventilation is provided by exhaust fans located in each room.

All animal racks are suspended from the ceiling and are removable. In the infectious building the animal holding and autopsy rooms are provided with drainage gullies where potentially contaminated wash water used in the room can be held for chemical disinfection before discharge to the sewer. The change room has a shower as well as facilities for disinfecting boots and waterproof overalls. All potentially contaminated materials exit via a double-doored autoclave. No cabinets are provided in the autopsy room, but the exhaust air is removed at grills located at the rear of the autopsy table.



LEGEND

1. Post-mortem room
2. Ventilated animal racks
3. Sterilizing
4. Cage washing

Figure 17. Floor Plan of a British Animal Isolation Area.

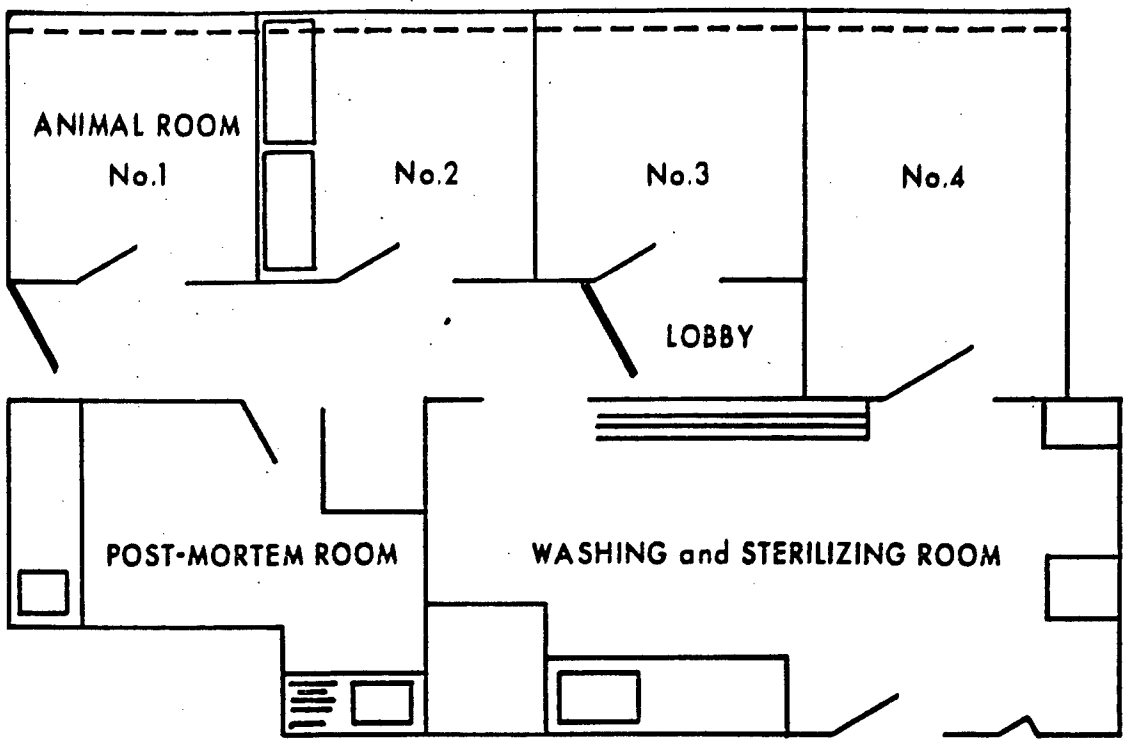
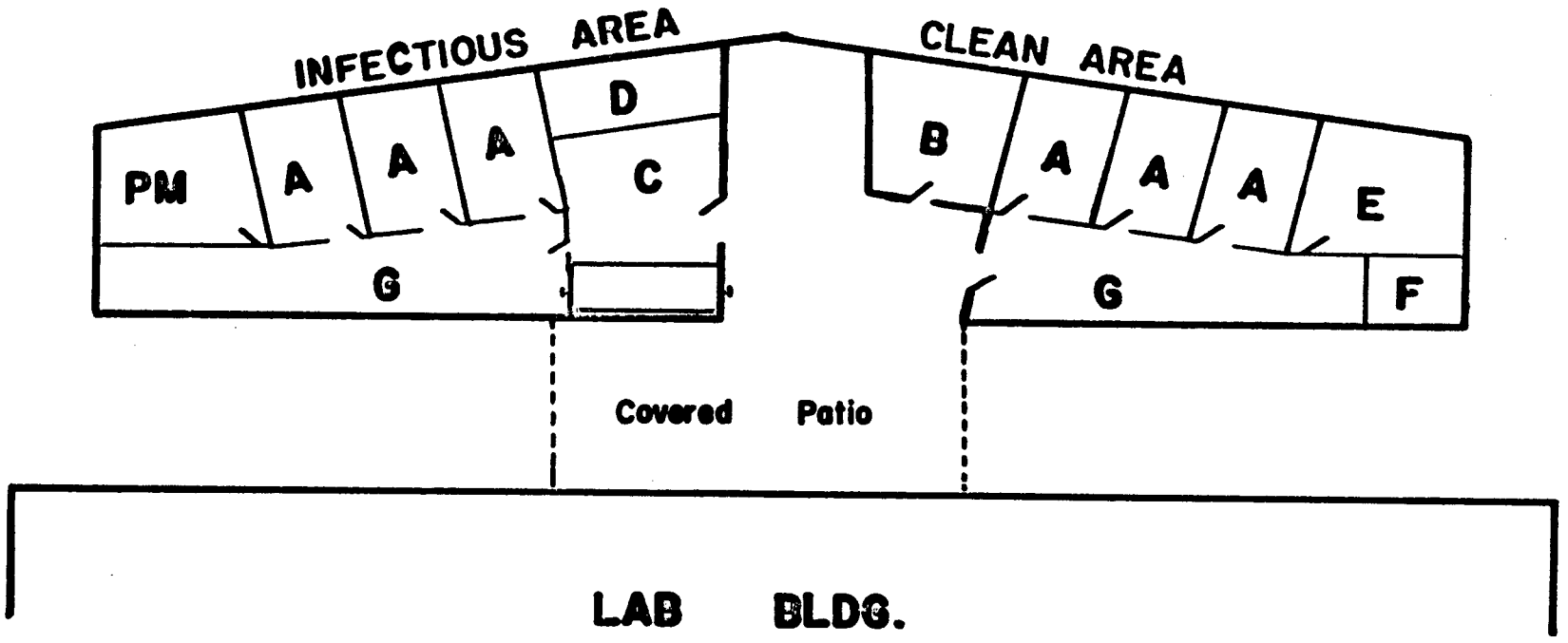


Figure 18. Floor Plan of an Animal House in England.

8. A German Virus Laboratory

A "high risk" virus unit has been recently completed in a large room of an existing German laboratory building. The unit is designed not so much to protect the workers from infectious risks, but to provide an area for work with virus infected animals where there is little chance of cross infection or cross contamination between rooms (Figure 20). The unit consists of three small, glass-walled laboratory rooms built in the center of a former classroom. As shown in the sketch, the direction of movement of personnel is controlled by a double-corridor system and separate entrance and exit change rooms. The clothing lockers forming the wall between the two change rooms have doors on both sides. No shower facilities are provided.

Both inlet and outlet air is passed through high efficiency bacterial filters. None of the personnel air locks are equipped with ultraviolet radiation, although UV is used in small equipment air locks leading to each room. Each glass-walled laboratory has ventilated animal cage racks



LEGEND

PM = Autopsy room
A = Animal-holding rooms
B = Clean storage
C = Change room
D = Utility room
E = Office
F = Toilet
G = Hallway

Figure 19. Floor Plan of an Animal House in Scotland.

(called Degastoria, see page 215) along one wall and a work bench along another. Foot operated telephones and sinks are provided in each room. All manipulations are carried out on the table top. A double-doored autoclave in the wall of the contaminated hall allows materials to be sterilized as they are passed to the washroom. A series of air locks separates this laboratory unit from an adjoining "medium risk" virus laboratory.

Shown in Figure 21, the "medium risk" laboratory was designed primarily for tissue culture operations. The air system is the same as for the "high risk" unit, and, as in that unit, no facilities are provided for sterilizing the exhaust filters before they are changed. A primary change room is provided where personnel change their shoes and put on laboratory coats. The walls of the laboratory rooms are plaster. Two of the rooms have secondary change rooms with showers. These two rooms may be used as one unit or as two units, each for a separate viral agent. Two rooms have equipment air locks with ultraviolet lamps. The dishwashing and storage area serves both the high risk and the medium risk laboratory units. No safety cabinets are provided.

9. A Norwegian Virus Laboratory

The general layout of the suites in a newly constructed Norwegian virus laboratory is shown in Figure 22. One enters the suite through an ultraviolet air lock which leads either to an office or to the laboratory. Two "sterile" rooms and a utility room join the laboratory. One of the "sterile" rooms is maintained at a negative air pressure. It contains a chemical fume hood (with ultraviolet lamps but no air exhaust filter) and is used for work with hazardous viruses. The other "sterile" room is at a positive air pressure and is used for maintenance of tissue cultures. Ultraviolet lamps are located over the tables in the "sterile" rooms. Tables, incubators, centrifuges, etc., are located in the central laboratory room. An upright deep freeze is mounted in the wall of this room. All table tops are of teakwood. A small anteroom leading off of the main laboratory contains a double-doored autoclave which reaches through to a service room accessible from the hall. Although many of the design features of the building provide less than maximum facilities for containment of infectious microorganisms, the layout of the suites is well planned and convenient for virus research. Their chief deficiency is the lack of a suitable ventilated safety cabinet in the negative pressure room.

a. Ventilation System

All motors, fans, and other equipment for the separate supply and exhaust systems are located in the attic. The ventilation rate in laboratory rooms is about eight changes of air per hour. Air pressure balance is maintained in each laboratory suite. The hallway air locks are maintained at a positive pressure, but there is no over-all control of air balance between different areas and floors. The building is completely

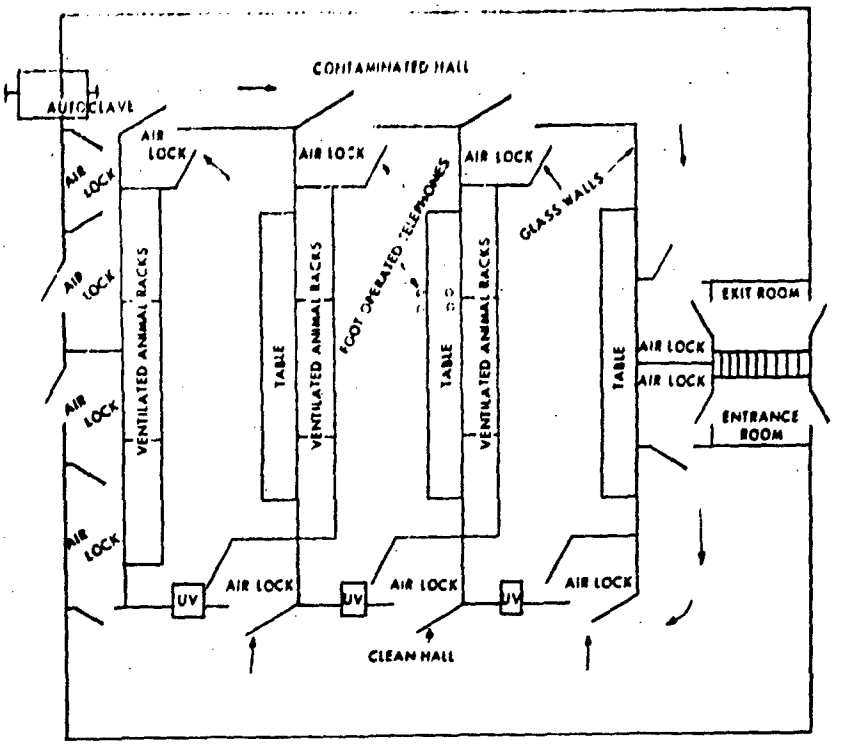


Figure 20. Floor Plan of a High Risk Virus Laboratory in Germany.

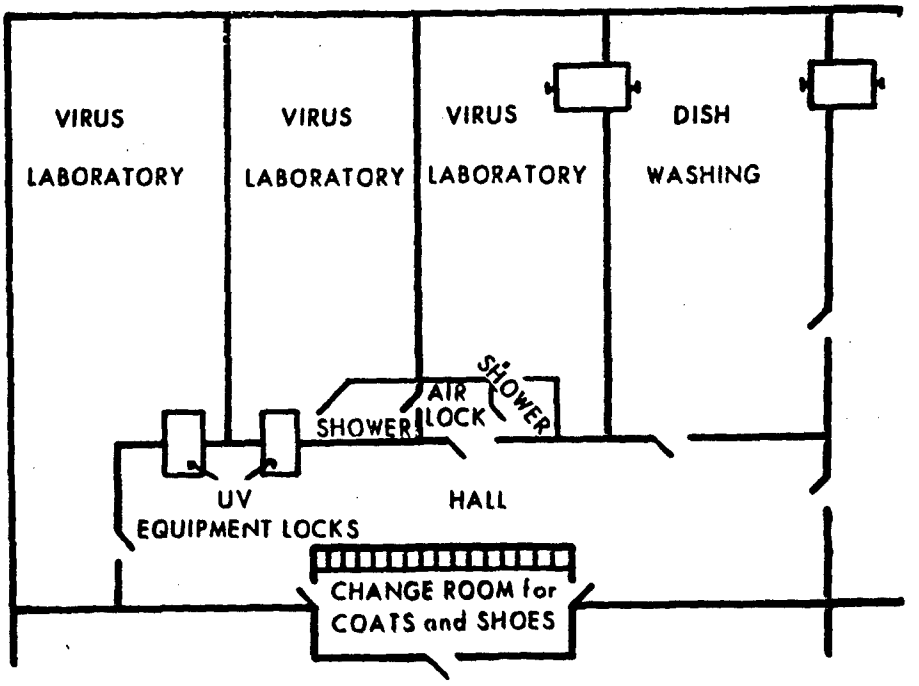


Figure 21. Floor Plan of a Medium Risk Virus Laboratory in Germany.

air-conditioned (unusual for this part of the world). Inlet air is dust filtered, heated or cooled, dehumidified, and then passed through bacterial filters. Exhaust air is discharged unfiltered from stacks extending ten meters above the top of the building. All air ducts are made of aluminum. Auxiliary heat is supplied in the laboratories by hot water pipes encased in the concrete floors. As a conservation measure, the ventilation air is reduced during the night.

b. Service Controls

An elaborate service control indicator panel in the basement indicates the operating condition of all incubators, refrigerators, deep freezes, and other electrical appliances in the building. An instantaneous temperature reading can be obtained by the building maintenance engineer from any of 150 locations throughout the building.

c. Change Rooms

Six change rooms which service the building are located in the basement. Unfortunately this proscribes any demarcation of clean and contaminated areas within the building.

d. Pipe Chases

Utility piping is located in vertical chases which open with heavy metal doors onto the corridors on each floor. The chases are not sealed between floors. Other corridor doors open to storage cabinets. Air ducts are located in horizontal chases above each corridor. The false ceiling of the corridors is made of sections of corrugated plastic material and is easily removed but not dust tight.

e. Windows

All windows in the building are double paneled and do not open to the outside. The inside panels may be opened with a special key for cleaning.

10. A Norwegian Tuberculosis Laboratory

Figure 23 is a sketch of a Norwegian tuberculosis laboratory which is a renovated lecture room provided with a balanced air system. All operations are carried out in the ten ventilated cabinets. In the center of the room one cabinet is provided for opening the specimens received by the laboratory. Other initial procedures are carried out in the other cabinets in this room. Three small rooms, each with a cabinet, are provided for isolation of procedures of higher risk. Unfortunately air withdrawn from the ventilated cabinets is discharged to the outside without filtration.

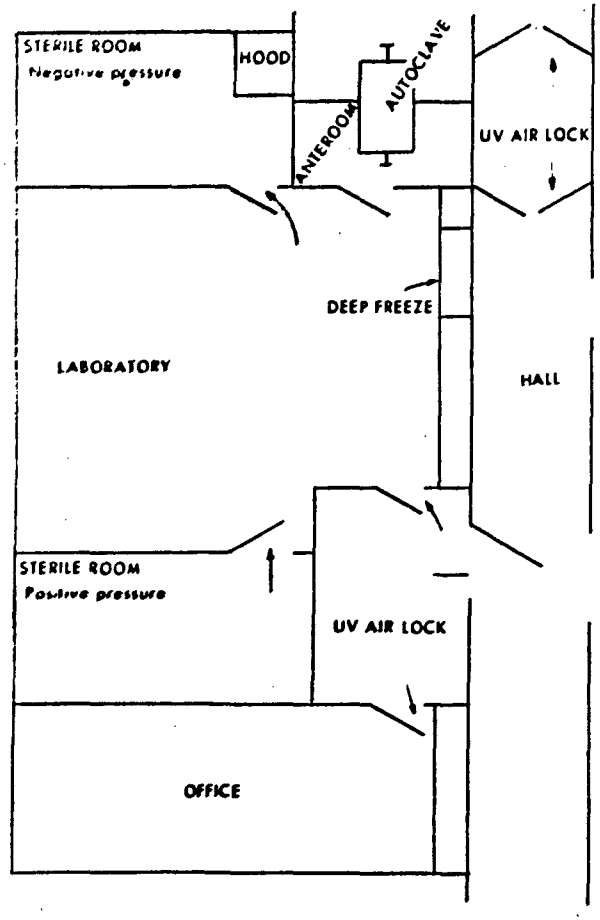


Figure 22. Floor Plan of a Norwegian Virus Laboratory.

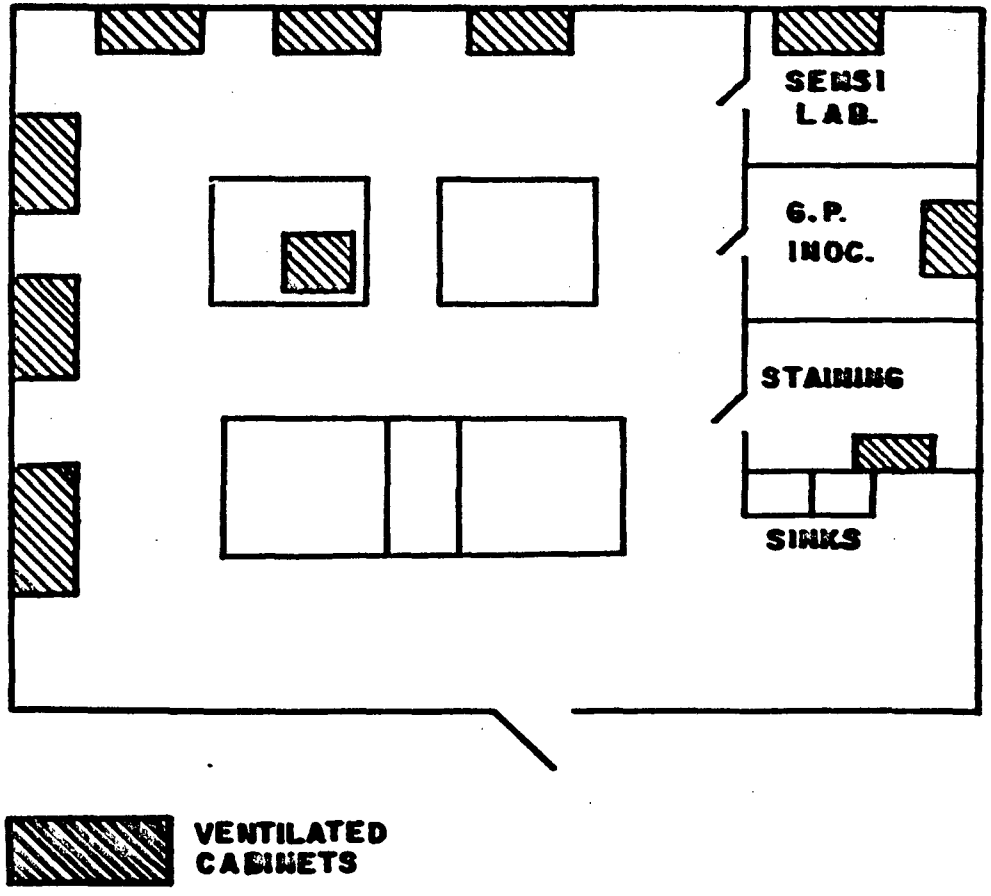


Figure 23. Floor Plan of a Norwegian Tuberculosis Laboratory.

11. Swedish Laboratories Under Construction

a. Gothenburg

A new complex of laboratory buildings being constructed in Gothenburg, Sweden will, upon completion in 1962, be one of the most up-to-date examples of special buildings and equipment designed to handle infectious microorganisms and to protect laboratory personnel. The safety program being planned by the laboratory officials promises to be equally outstanding. In years to come these laboratories should indeed be a show place for microbiological safety.

The construction is a joint endeavor by the Swedish Government and the Municipality of Gothenburg. Laboratory and teaching facilities will be provided for the University of Gothenburg Medical School and the Gothenburg Municipal Bacteriological Laboratory. I estimate that the complete facility will accommodate a working staff of about 400 people.

The complex includes seven buildings or wings of buildings. The central structure consists of:

(1) A square-shaped wing for student laboratories and lecture rooms. This structure has five floors and two basements with a total of approximately 1960 square meters of floor area.

(2) A central rectangular shaped bacteriology building for public health and medical diagnostic laboratories. There will be six floors and two basements for a total of 6608 square meters of floor area.

(3) A laboratory extending at right angles to (2) above will provide research laboratories for the medical school. It will have four floors and two basements with a total of 3234 square meters of floor area.

(4) Also adjoining (2) above will be a laboratory used primarily for diagnostic virology. This structure is approximately equal in size to the wing for student laboratories and lecture rooms and will extend four or five stories above ground.

To the rear of the main block of buildings is a four-story building for normal animals and animals challenged with bacterial agents. A two-story wing attached to this structure provides the holding and autopsy area for virus infected animals. The last building in the complex is a small, single-story laboratory for the production of BCG vaccine.

Some of the design features of the new buildings are:

(1) No air is to be recirculated. Risk areas will be provided with separate air systems and exhaust air will be filtered. The single exception is that air from ventilated animal cages will be exhausted without treatment. Ventilation rates will be about ten changes per hour for

laboratory rooms and 20 changes per hour for animal areas. Particular attention will be paid to the air pressure balance between areas.

(2) Sewage from the virus areas and other risk areas will be pasteurized and chlorinated.

(3) Change rooms will be provided for almost all areas. Technicians and professional personnel usually will have separate change rooms. All personnel, including medical students, who enter infectious areas will be required to make a complete change of clothing upon entering and to shower before leaving. Some risk areas will be situated so that personnel are required to traverse two sets of change rooms. As a luxury feature for employees a saunna, or Finnish steam bath, will be provided in the basement of the main building.

(4) In the design extensive use has been made of personnel and equipment air locks. All will be equipped with ultraviolet lamps.

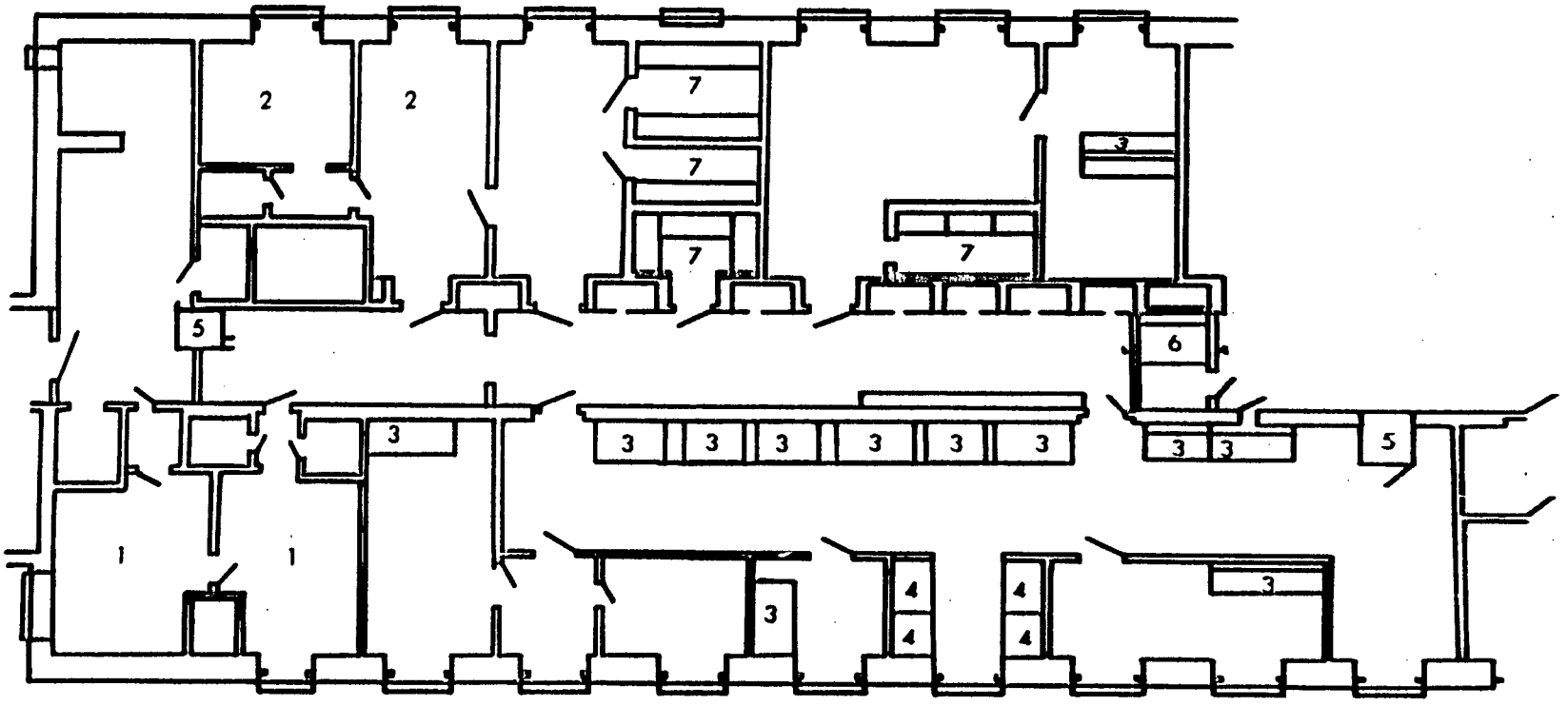
(5) All infectious laboratory operations will be carried out in ventilated cabinets and all infected animals will be held in ventilated cages. Wide use will be made of disposable, cardboard animal cages. The average sized infectious animal room will accommodate 180 ventilated cages. Three guinea pigs can be held in each cage.

(6) Double or triple corridor systems have been used in the design of all animal rooms. Personnel will enter each room from a clean corridor and exit via a contaminated corridor. In some instances the corridors will be outside porches. The third corridor, when used, is below the animal rooms.

(7) Facility piping in most of the buildings will run from floor to floor through vertical pipe chases located in the corridor walls and in the outside walls.

(8) A high risk laboratory area is to be provided for aerobiological studies.

The tuberculosis laboratory will occupy approximately half of one floor of the bacteriology building. Figure 24 shows the general room arrangement and the location of ventilated cabinets and other equipment. Thirteen ventilated cabinets and four ventilated centrifuges will be provided. All personnel will enter through the clean and contaminated change rooms. Clean supplies delivered to the isolation unit enter through an ultraviolet air lock at the end of the corridor nearest the office. Specimens to be investigated are passed through an air lock directly into a ventilated cabinet where they are opened. All contaminated and discard materials will be sterilized in the double-doored autoclave and passed to the clean area for washing, resterilizing, etc. Unfortunately, this is the only autoclave in the isolation unit. Notice that a separate room or area is provided for each laboratory function.



LEGEND

1. Change rooms
2. Offices
3. Ventilated cabinets
4. Centrifuge cabinets
5. UV air locks
6. Autoclave
7. Incubators

Figure 24. Floor Plan of a Swedish Tuberculosis Laboratory.

The triple-corridor isolation wing for virus infected animals has corridors on either side and below each animal suite. Figure 25 shows two of the three corridors with the interpositioned animal holding and autopsy rooms. Corridor A is used only by professional personnel for access to the autopsy and animal rooms. Professional personnel enter and leave via corridor A and do not enter corridor B or corridor C below. Corridor B is used by animal attendants who feed and water the animals, clean the rooms, and prepare animals for injection or autopsy. These attendants do not enter corridors A or C. Corridor C (not shown) is located in the basement below the animal holding rooms. A small elevator connects each animal holding room with the subterranean corridor. The elevators are used only for the exit of contaminated cages and bedding, animal caracsses, and other contaminated materials. Connected with corridor C in the basement are rooms with equipment for sterilizing and washing cages and incinerating bedding and animal carcasses. Corridor C is considered to be of higher risk than the other two corridors, and personnel working here do not enter the other corridors.

As shown in Figure 25, each autopsy room is equipped with a ventilated autopsy cabinet. Ventilated cage racks are provided in each animal holding room. A lock for the decontamination of hands and shoes is placed between each animal holding room and corridor B.

b. Stockholm

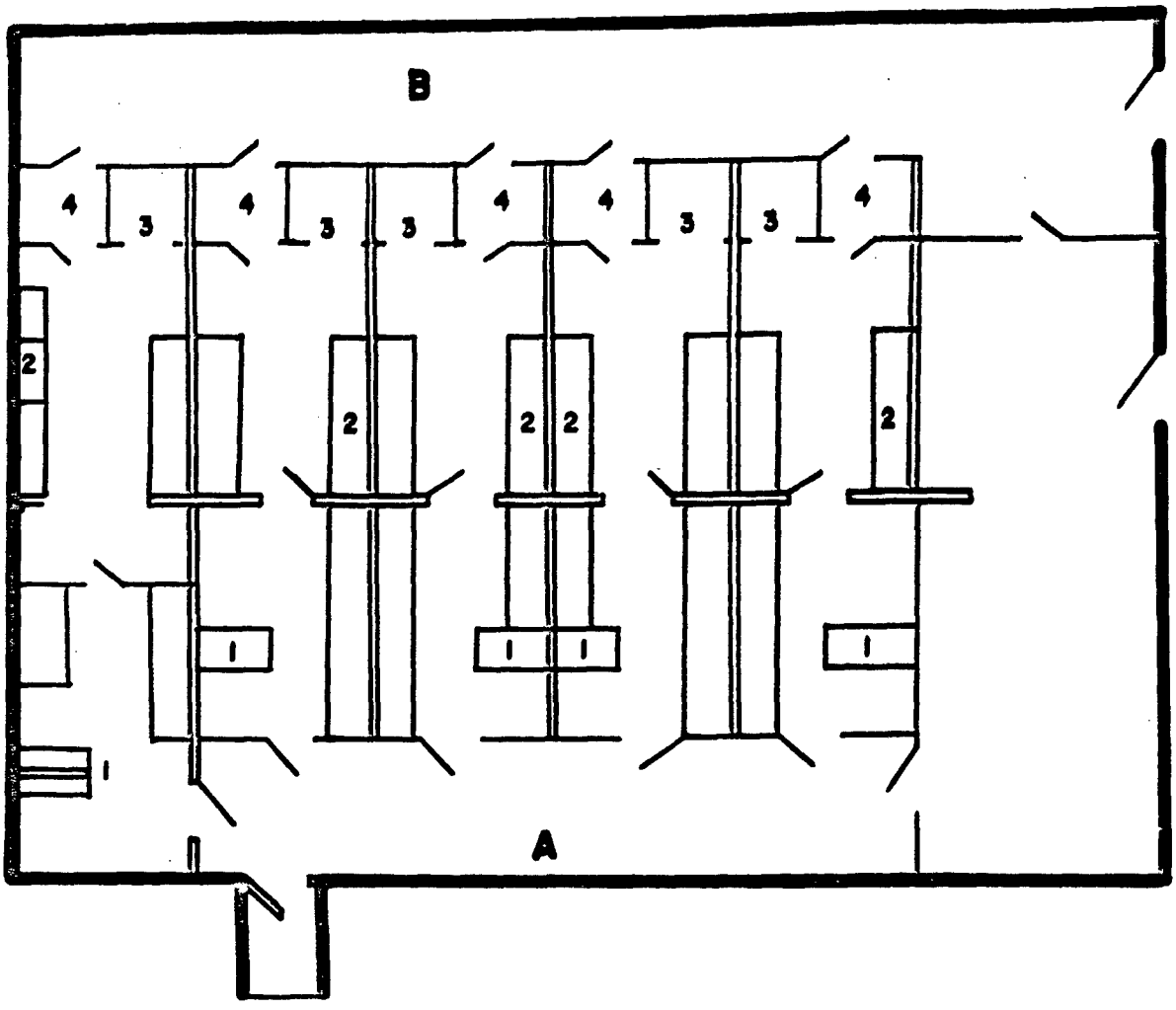
Two new laboratory buildings being built at the Swedish State Bacteriological Laboratories in Stockholm have many design features in common with the Gothenbrug laboratories. Some specific design features are as follows:

(1) Only the corridor and outside walls bear weight. Most ceilings and non-weight-bearing inside walls are made of sheets of open-pore, expanded concrete (Siporex) which is delivered in sections approximately two by three meters. This material is lightweight and can be cut with ordinary equipment. Exposed surfaces of the prefabricated walling will be sealed with a plastic paint. Interior walls will be relatively easy to move.

(2) All potentially contaminated exhaust air will be filtered. Air from highly infectious animal rooms will be incinerated. Each floor of each building will have a separate, non-recirculating air system. Much of the supply air will be filtered. Auxiliary heat for laboratory rooms will be supplied by hot water pipes in the floors.

(3) Potentially infectious sewage will be pasteurized.

A building for infected animals presently under construction uses the three-corridor system and contains 2550 square meters of floor area. Many of the rooms will be provided with ventilated animal cages and ventilated autopsy cabinets.



LEGEND

1. Autopsy cabinets
2. Ventilated cage racks
3. Elevators
4. Decontamination locks

Figure 25. Floor Plan of a Triple-Corridor Animal Isolation Wing.

A new virology building will have a basement and three floors, providing a total of 2500 square meters of floor space. The standard room size is three by five meters. Figure 26 shows the typical room arrangement for a three-room suite to be used for infectious viral operations. A locker room is provided on each floor of the building. The suite has an additional locker room for the changing of laboratory coats and shoes. In this building a complete change of clothes and exit showers will probably not be required. Supply air to each room comes from vertical pipe chases on the outer walls. Exhaust ducts are located in the corridor pipe chases. Exhaust air filters are located at the point of exhaust from each room. In the suite illustrated, the doors to the two laboratory rooms have been replaced with ultraviolet equipment locks. The locks are designed so that they can be easily replaced with a door if the room is to be converted to a clean laboratory. A ventilated cabinet will be provided for hazardous operations. The sterile room will be used primarily for the maintenance of tissue cultures.

C. AIR VENTILATION FILTRATION AND STERILIZATION

In about half of the laboratories there was some type of mechanical air ventilation system. In a number of instances only a portion of the building was ventilated. Systems in 21 laboratories provided a positive air pressure in the rooms, while 19 laboratories had negative room pressures. Very few of the ventilation systems were of the recirculating type. Table XXX shows the frequency of treatment of ventilation air by filtration, ultraviolet irradiation, and heat sterilization. In general, inlet air was treated more frequently than outlet air, although in some laboratories both were treated.

TABLE XXX. TREATMENT OF AIR IN 102 INFECTIOUS DISEASE LABORATORIES

BUILDINGS USING	PER CENT
Filters for treatment of air	33
Filters for inlet air	24
Filters for outlet air	15
UV to treat moving air	21
UV to treat inlet air	13
UV to treat outlet air	8
Heat to sterilize outlet air	11

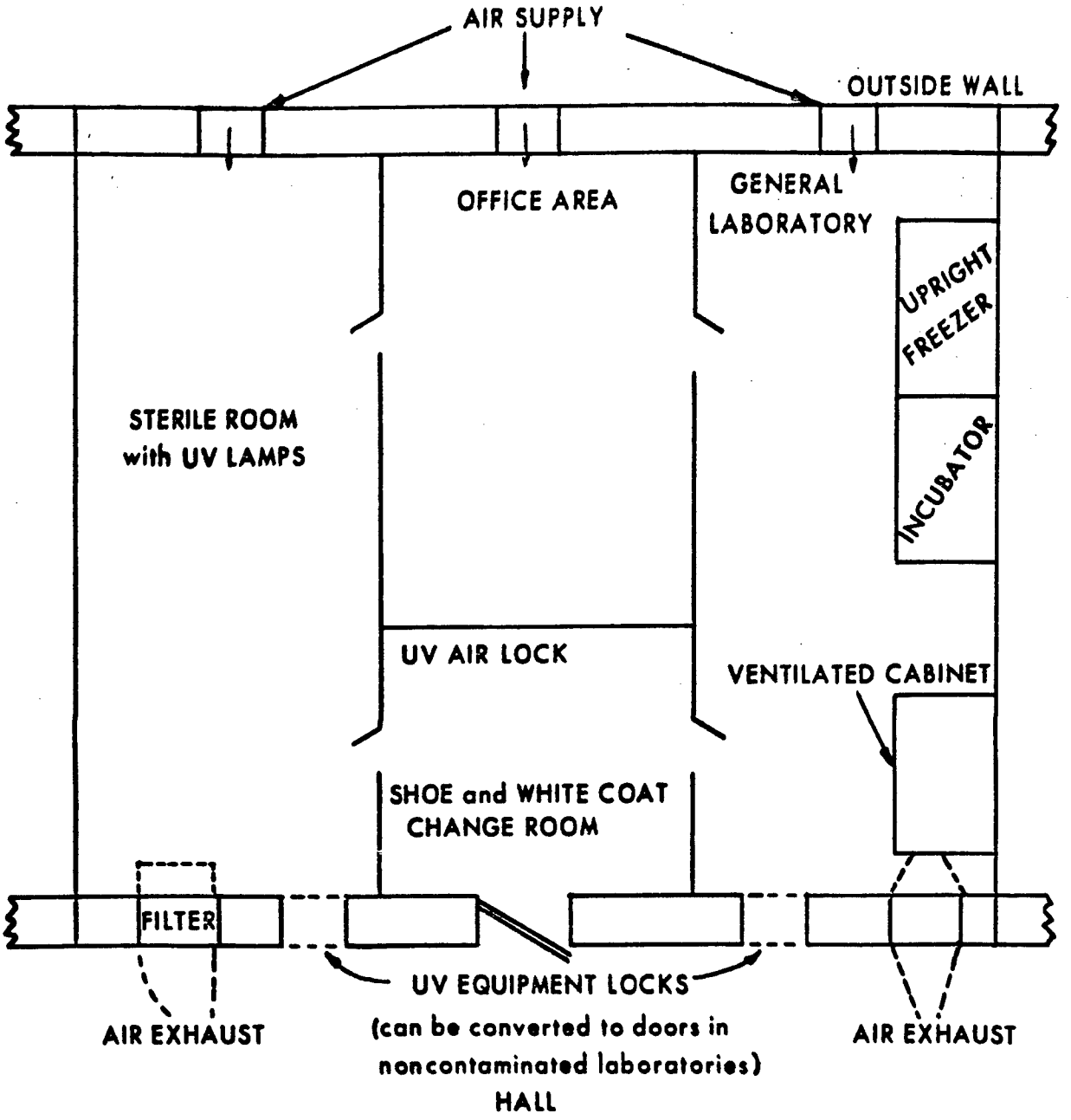


Figure 26. Floor Plan of a Swedish Virus Laboratory Suite.

Ventilation rates varied from a low of four to a high of 20 changes of air per hour. For laboratory rooms a ventilation rate of five changes per hour was typical. In many institutions laboratory rooms were ventilated, but the animal quarters were not. However in the most modern buildings, when the animal rooms were ventilated, a rate of 10 to 15 changes per hour was typical.

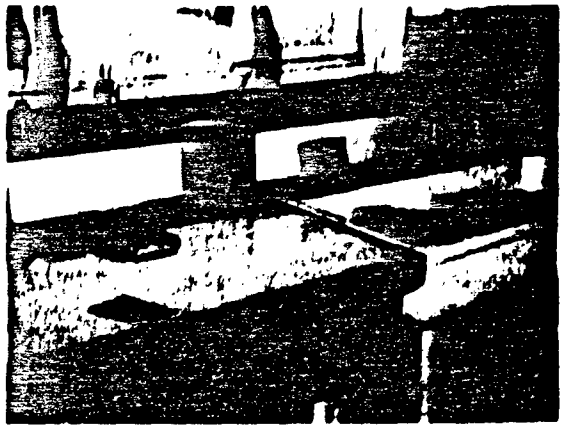
Systems supplying air to virus vaccine production laboratories or animal units usually combined several treatment methods. A typical system utilized electrostatic precipitators, air filters, and ultraviolet irradiation. By contrast, when exhaust air was treated usually only one treatment method was used.

In general most directors felt that there was little or no need for treating air exhausted from infectious disease laboratories. They felt that the dilution of the potentially contaminated air with fresh outside air was sufficient to eliminate all risks. However, several directors stated that it was best to have exhaust filters for "political purposes." Thus the institute is protected in case there is criticism from the surrounding community.

The design features of room ventilation systems varied considerably. In most modern buildings, room ventilation was accomplished by means of separate air inlet and outlet ducts located above head level and some distance apart on the ceilings or walls of the rooms. However in several laboratories air was admitted at the ceiling and removed at floor level. In one laboratory the reverse procedure was followed. Figure 27, A, shows air exhaust ducts located at the rear of the tables in an autopsy room as seen in several laboratories. In one recently completed building, room ventilation was inadequate because the air inlet and outlet ducts were close together and allowed a short circuit of the air (Figure 27, B). In several U.S. laboratories the air louver device shown in Figure 27, C, was employed. Air enters the room through one louver opening and is exhausted from the other. Exhaust air filters were sometimes located on the opening of the air exhaust duct in the room as illustrated in Figure 27, D. This arrangement makes it difficult to decontaminate the filters before they are changed.

Examples of plenums for the treatment of exhaust air with ultraviolet radiation are shown in Figure 28. In each hot cathode type ultraviolet lamps were employed. Only one of the four had been tested to determine the efficiency of the treatment method.

Other air treatment methods are illustrated in Figure 29. Picture A shows several cotton pad filter units of a type frequently seen in Europe. Large rolls of the filter material are supplied, and the filters are changed by laboratory or maintenance personnel. Picture B shows two filter units in a Swedish laboratory which are similar to units developed by the U.S. Army Biological Laboratories. Another Swedish laboratory used the cartridge-type filters shown in Figure 29, C. These were developed at the laboratories of



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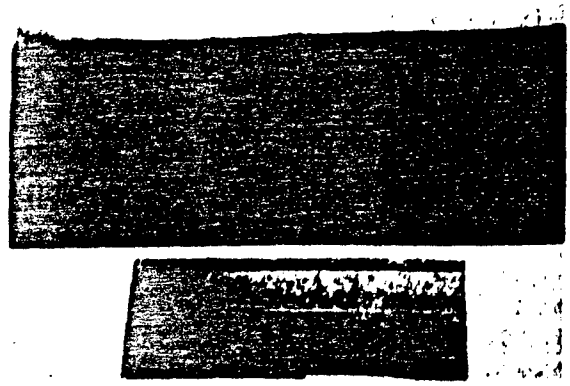
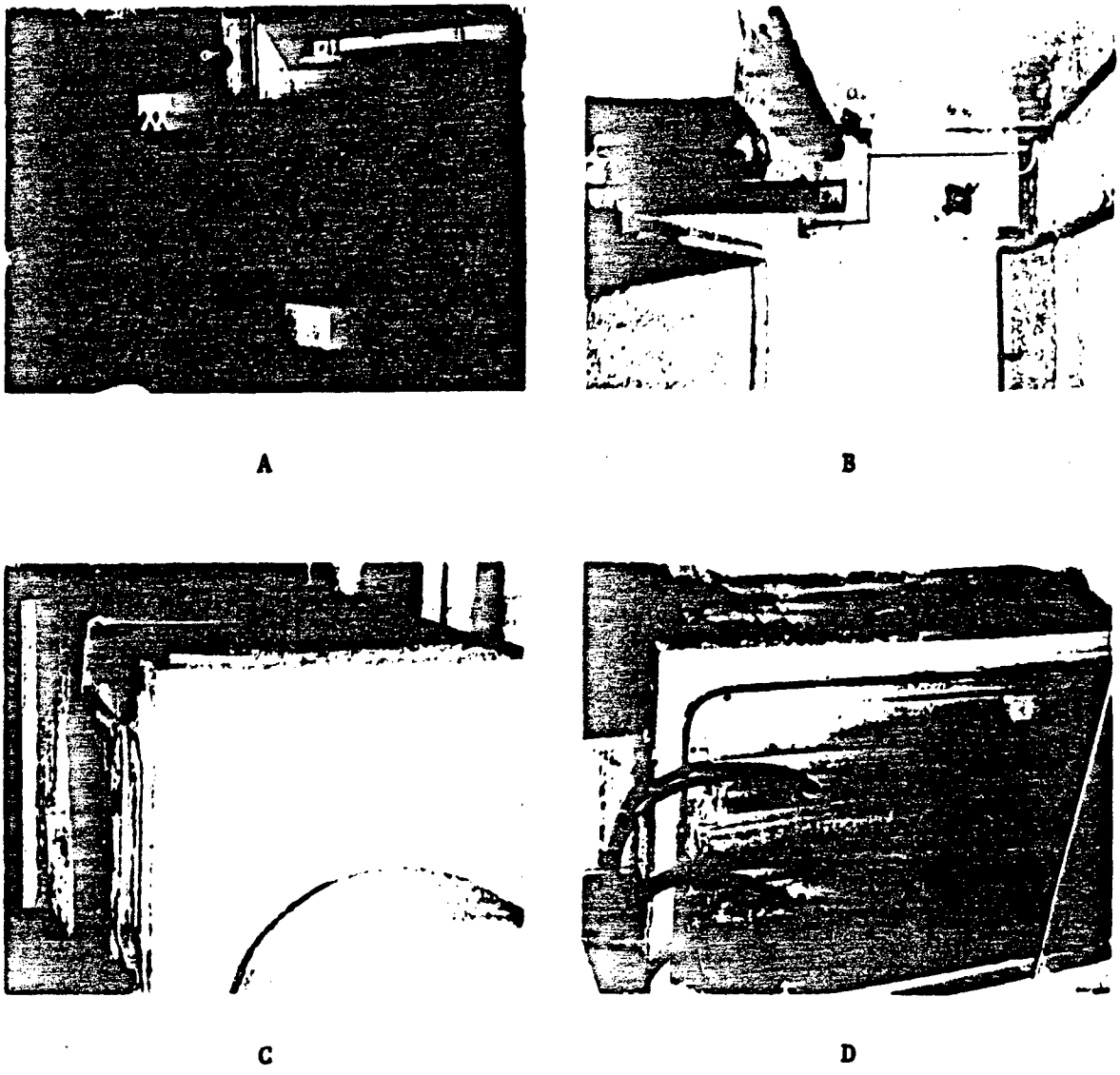


B

C

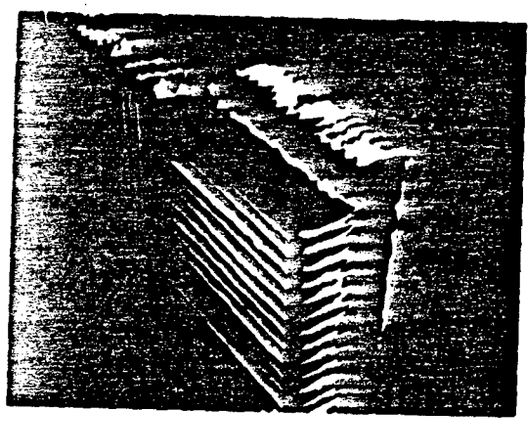
D

Figure 27. Air Exhaust Ducts.
A. Exhaust Louvers at Rear of Autopsy Table.
B. Inlet and Outlet Louvers Adjacently Located.
C. Double Louver Air Device.
D. Air Filter on Exhaust Duct.



A B C D

Figure 28. Ultraviolet Irradiation Plenums.
A. Double Plenum System for Room Exhaust Air.
B. Plenum to Treat Air from Animal Cages.
C and D. Plenums to Treat Air from Ventilated Cabinets.



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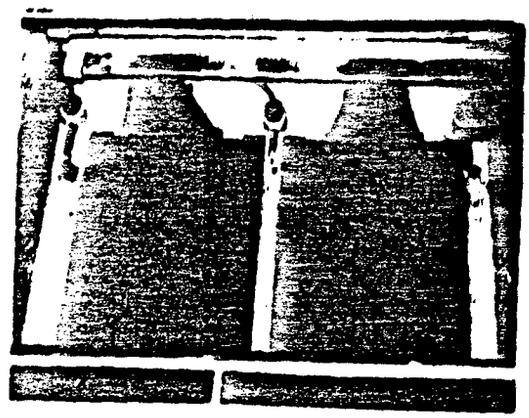

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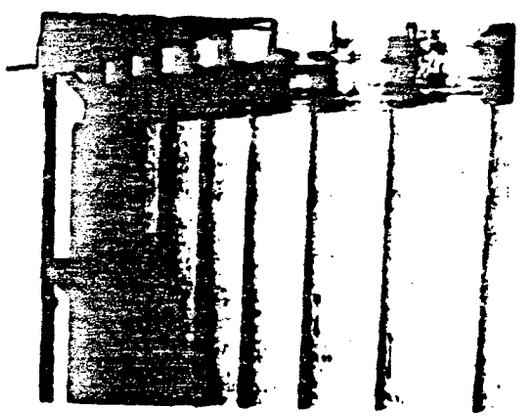

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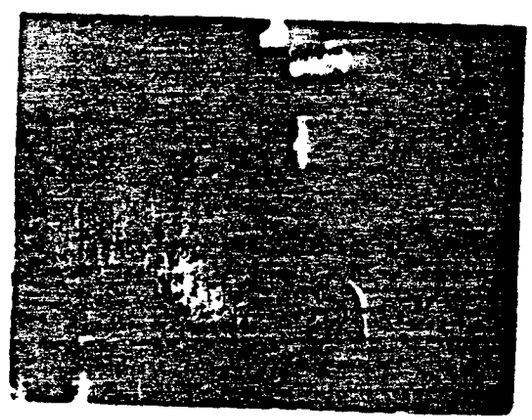


D

Figure 29. Air Treatment Systems.
A. Cotton Pad Air Filters.
B. Spun Glass Filter Units.
C. Cartridge-Type Air Filter Units Packed with Cotton-Asbestos Material.
D. Gas-Fired Air Incinerator.

the Microbiological Research Establishment in Porton, England. A typical gas-fired air incineration unit is shown in picture D. This unit was used to sterilize the air from cabinets and rooms in which highly infectious viral agents were used.

Observations on the design features of air ventilation and air filtration systems in approximately 50 laboratory buildings permit the following list of features frequently overlooked:

1. Ventilation rates are often inadequate.
2. Critical areas, such as animal rooms, are often not ventilated.
3. Air pressures in risk areas are frequently positive to areas of no risk.
4. Treatment of air supplied to infectious areas is often considered to be more important than the treatment of exhaust air.
5. Few air treatment systems have been adequately tested.
6. Few air treatment system designs provide adequate means for sterilizing exhaust filters, and testing ultraviolet lamps.

H. AIR LOCKS AND DUMB-WAITERS

Equipment air locks or pass-boxes are useful containment devices in laboratories because they provide a means of passing equipment to and from a room without the entry of personnel and without the necessity of opening hallway doors. Air locks between laboratory rooms are especially serviceable in infectious operations which can be arranged so that the work flows from room to room in assembly line fashion. Routine diagnostic operations and vaccine production are two areas in which it is often possible to arrange the work in this manner. The technique usually makes it possible to limit the size and the number of persons involved in the more hazardous operations. For example, in an European laboratory handling a large number of samples for the detection of tubercle bacilli, the work was arranged in separate but adjoining rooms as follows:

1. Receiving and recording of samples received.
2. Digestion and concentration of sputum samples and inoculation of growth media.
3. Incubation of growth media.
4. Examination of growth media.
5. Culture sensitivity tests.

Each of these operations undoubtedly involves a different degree of risk, with the greatest occurring in the last operation. In many laboratories the operations listed above were done in one or two rooms without separation of operations and without the benefit of ventilated cabinets. The assembly line concept with materials, but not people, passing from room to room through in-the-wall air locks provides an efficient means of improving isolation in infectious disease laboratories. Equipment air locks of this type were found in ten per cent of the laboratories. Figure 30, A shows the use of an air lock in the production of virus vaccines. In this instance nonhazardous operations such as candling and preparing eggs for

inoculation were physically separated from subsequent risk operations such as inoculation, incubation, and harvesting. The air lock illustrated was equipped with ultraviolet lamps and a door interlocking device which prevented the opening of both doors at the same time. Figure 30, B shows an air lock used in another virus laboratory to pass materials from the hallway to the laboratory room. No ultraviolet is provided in this case.

In multi-storied laboratory buildings the use of dumb-waiters or small equipment elevators provides a natural expedient for the movement of glassware and other materials between laboratory rooms and dishwashing or storerooms. However, when one of the rooms serviced is a potentially infectious area, the dumb-waiter, if not properly designed and controlled, constitutes an undesirable means of spreading contamination. Of the 12 dumb-waiters inspected in infectious laboratory buildings, not one was properly designed to prevent spread of contamination to non-laboratory areas. None was equipped with ultraviolet or any other device to prevent the pumping of infectious air from area to area. In some instances the direction of air flow through the open elevator shaft was toward the clean areas. None of the dumb-waiters had been safety tested. In one laboratory a dumb-waiter serviced a laboratory room, an animal room, and a dishwashing area.

Figure 30, C shows a dumb-waiter located in the hall of a new European laboratory. The dumb-waiter shown in Figure 30, D connects a laboratory room with a service area where all autoclaving of infectious discards was done, as well as the preparation of sterile materials for laboratory use. This dumb-waiter was compartmentalized for contaminated and sterile materials.

In general it would seem desirable to avoid the use of dumb-waiters in infectious disease laboratories unless they are properly engineered and shown not to spread contaminants between areas of unequal risk.

I. SEWAGE TREATMENT SYSTEMS

Nine of the 102 existing laboratories had some type of sewage treatment system. At two other laboratories treatment systems were being included in buildings under construction (both in Sweden). None of the U.S. laboratories visited had sewage treatment systems. Of the eleven treatment systems, only the one at the Microbiological Research Establishment in England was designed to sterilize liquid effluents; the others provided only pasteurization. Among these, the following specific treatments were included:

1. 60°C for 30 minutes
2. 80°C for 1 hour
3. 80°C for 2 hours
4. 90°C for 2 hours
5. 90°C for 3 hours

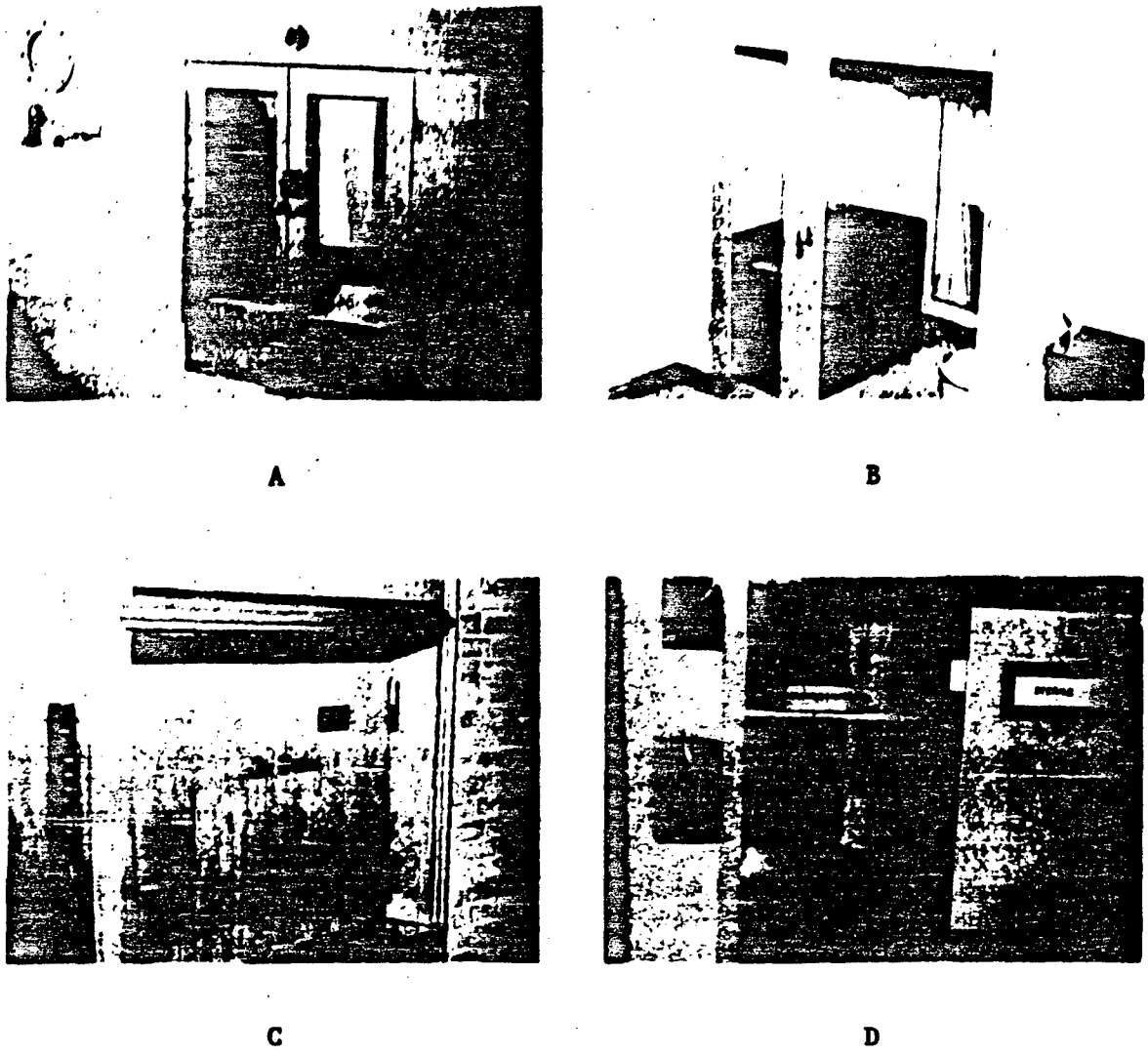


Figure 30. Air Locks and Dumb-Waiters.
A. UV Equipment Air Lock.
B. Equipment Air Lock Without UV.
C. Dumb-Waiter in a Hall.
D. Laboratory Dumb-Waiter.

6. 90°C for 3 hours and then chlorinate
7. 100°C for 10 minutes
8. Heat to boiling and then let cool.

It is apparent that no one treatment regime has been universally accepted. Six of the ten pasteurization systems were intended specifically for the treatment of sewage from animal and autopsy rooms used for the production or safety testing of poliomyelitis vaccine. One system had been used specifically to treat drainage from an aerosol vessel used with tubercle bacilli. The remaining three systems handled sewage from laboratories and animal rooms where a variety of infectious agents were handled.

All of the systems used steam as the source of heat and all treatment was done on a batch basis. That is, a tank full of liquid was collected, treated, and then dumped. The distribution of the systems by countries was as follows:

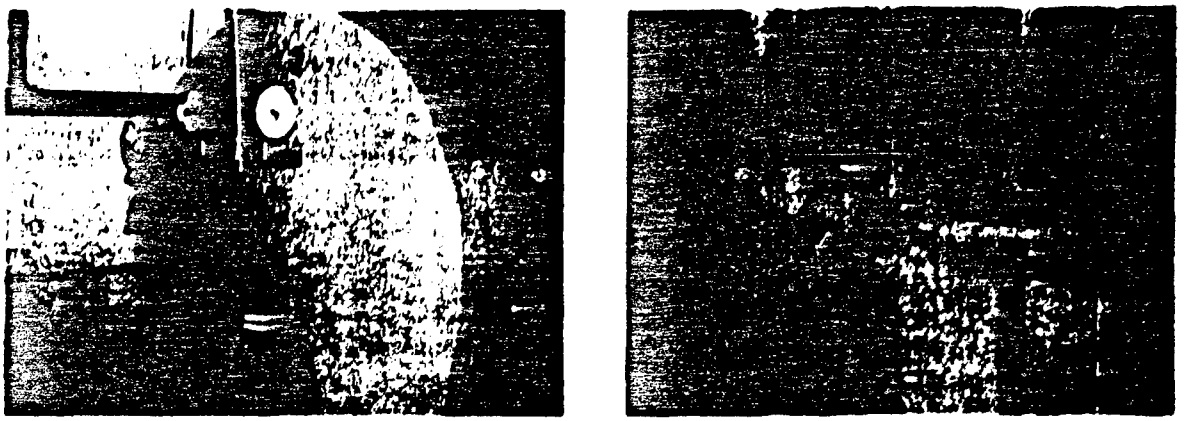
England	- 3
Germany	- 2
Sweden	- 5
Switzerland	- 1
Total	11

The system designed to sterilize effluents was rather complex, while others consisted primarily of a collection tank which could admit steam under pressure. Two pasteurization systems and one sterilization system are described below:

System A - Liquid drainage from the monkey holding and autopsy rooms flowed directly to a large concrete vat about 15 by 15 by 4 feet located in the basement. This vat had a loose fitting metal top, and was cleaned by hand every six months. At appropriate intervals a worker operated a pump which delivered sewage from the vat to a 500-gallon metal tank. (Figure 31, A). An electrically operated probe within the vessel rang a bell to indicate when the proper amount of sewage had been pumped in. Then steam under pressure was admitted to the tank until the temperature reached 90°C. The liquid was held at this temperature for two hours. After treatment the sewage was cooled by mixing it with raw river water and then the mixture was discharged into a nearby river.

System B - This smaller system used the batch treatment principle but was operated automatically. Two tanks were used so that one could be collecting effluent while the other was under steam pressure. All indicating controls and switches were located on an instrument panel in the laboratory. Each tank of sewage collected was heated to 100°C for ten minutes (Figure 31, B).

System C - A flow chart of a sewage sterilization system is shown in Figure 32. Multiple units of the type illustrated are used to sterilize liquid effluents from showers, animal rooms, and aerobiology laboratories.



A B

Figure 31. Sewage Treatment System Tanks.
A. 500-Gallon Steam Treatment Tank.
B. Double Tank Treatment System.

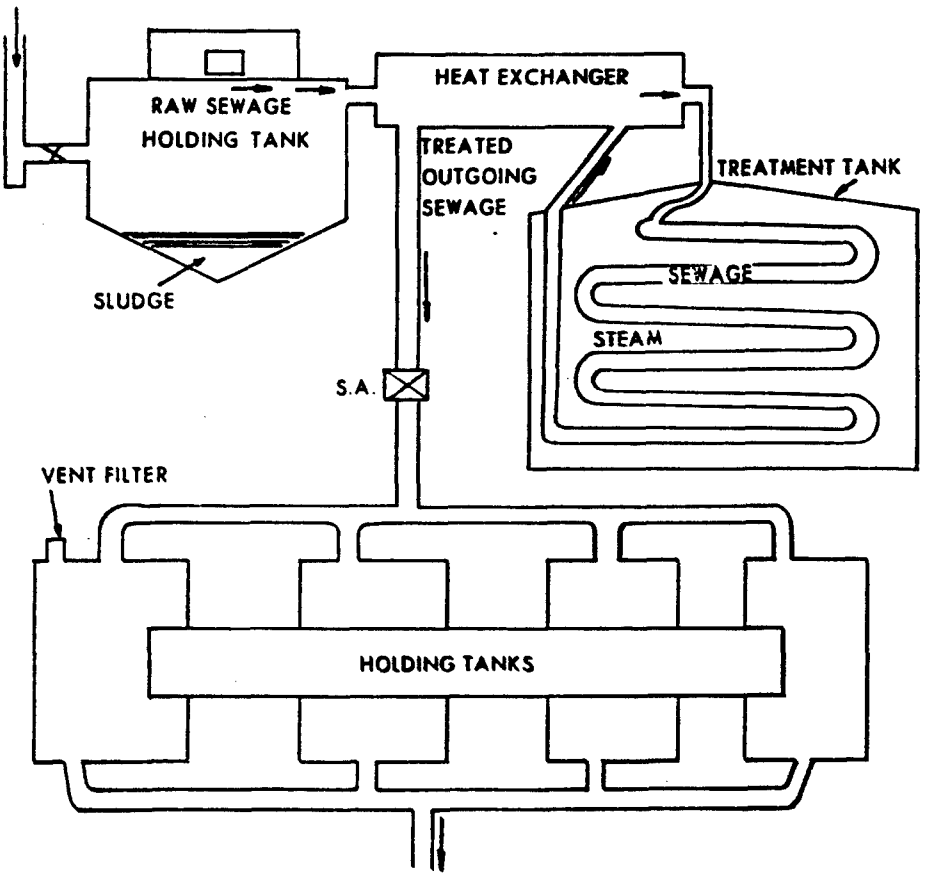


Figure 32. Sewage Treatment System Flow Chart.

Essentially the system operates as follows: Waste water flows from the rooms above through all-welded drain lines to a contaminate holding tank. When the tank is about three-fourths full, treatment is started. A pump pushes the effluent from the holding tank, through a heat exchanger, to the 1000-gallon treatment tank which is filled with steam under a pressure of about 40 psig. The liquid flows through a continuous pipe system inside the treatment tank. The flow rate is slow and the sewage is exposed to heat for about 30 minutes. Upon leaving the treatment vessel the hot sewage passes through the heat exchanger where it is cooled by the cold, incoming effluent.

When the treated material leaves the heat exchanger it passes the sampling adapter and is then discharged into one of four clean holding tanks. Here the treated material is held until the results of a sterility test are obtained (48 hours). Usually liquid is put in only three holding tanks and the fourth, which has an air vent with a filter, is used as a ballast tank for displaced air. If the biological test is satisfactory the contents of the tank are dumped — if not, the effluent is routed back to the steam vessel and treated again. The failure rate is about two per cent. No attempt is made to keep the treated liquid in the holding tanks in a sterile condition. The test criteria is that it should be sterile when it passes the sampling adapter The samples are taken at all times when material is being treated. The sampling arrangement is such that several drops from each gallon of treated sewage is sampled.

Most laboratory directors felt that it was difficult to justify the expense of treatment of sewage from infectious disease laboratories. In view of this, it was surprising to find as many treatment systems as were found. It is also significant that the majority were for sewage possibly contaminated with poliomyelitis virus rather than with brucella, tularemia, and tubercle bacilli. Several laboratory directors stated that regulations for the manufacture or testing of poliomyelitis vaccines were involved or, at least, that the presence of a system was evidence that everything was being done to assure the sterility of the product. In other words the systems sometimes served political purposes. Most directors agreed, however, that when certain disease agents, including animal agents, were used or when large-scale culture operations were carried out, treatment of the laboratory sewage should be recommended. Under normal circumstances most laboratory people saw little justification for the treatment of hospital sewage.

J. MISCELLANEOUS BUILDING DESIGN FEATURES

Table XXXI shows the frequency of some safety design features in the laboratory buildings inspected. Of those features listed, the most frequent was the use of isolation cubicles for separating certain laboratory operations from the other work going on in that room. Glass viewing windows into laboratory rooms were also rather common, particularly in the newer laboratory buildings.

TABLE XXXI. SAFETY DESIGN FEATURES OF 102 LABORATORY BUILDINGS

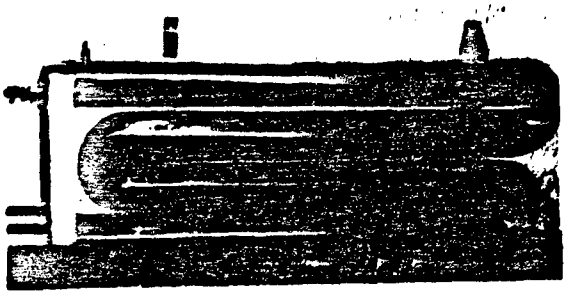
ITEM	PER CENT OF LABORATORY BUILDINGS HAVING FEATURE
Change rooms	23
Isolation cubicles	46
Ventilated	27
Nonventilated	19
View windows in rooms	41
Speaking diaphragms	6
UV door barriers	17
UV air locks	27

A number of miscellaneous laboratory design features are illustrated in Figures 33, 34, and 35.

This stainless steel sanitary radiator (Figure 33,A) in a Swedish infectious disease laboratory was designed for easy cleaning. Brackets hold the tubing away from the wall so that the rear surfaces can be reached. Low voltage heating wires on the inner walls of a walk-in incubator are the source of heat (Figure 33,B). Incubators of this type are being used in the U.S. and in Scandinavia. Figure 33, C shows a Finnish laboratory where the facilities were brought to island-type laboratory tables from overhead. Unfortunately, the expanded metal duct work is difficult to clean and to decontaminate. Figure 33, D shows an intercommunications system used in a German virus laboratory. It also serves as a telephone, allowing calls to be received without touching the instrument.

Figure 34, A and B show speaking diaphragms. A metal ring enclosing a thin sheet of plastic material allows easy communication between the office and an egg vaccine unit at a British pharmaceutical firm (Figure 34,A). A similar speaking diaphragm in the sliding door to a small isolation laboratory is shown in Figure 34, B. Figure 34, C shows a pass-through door which leads to a room housing infected animals. Materials can be passed through the small door thereby avoiding the necessity of opening the larger one. A distilled water station is located in the hall of a number of laboratory buildings (Figure 34,D). Each station provides distilled water for a number of laboratories, thereby avoiding the expense of piping distilled water to each laboratory.

Figure 35, A illustrates a method used in Sweden for bringing service facilities to the laboratory table top. The facilities are located in the channel along the outside wall of each laboratory. The tables can be easily moved because none of the facility outlets attach to them. The sink unit is readily moved because it connects to the drain by means of a rubber hose. Removable panels allow access to the piping. Foot-operated sinks are found frequently in the more recently constructed laboratory buildings (Figure 35, B and C). Figure 35, D shows a homemade device for delivering liquid soap by knee pressure using an automobile windshield washing apparatus.



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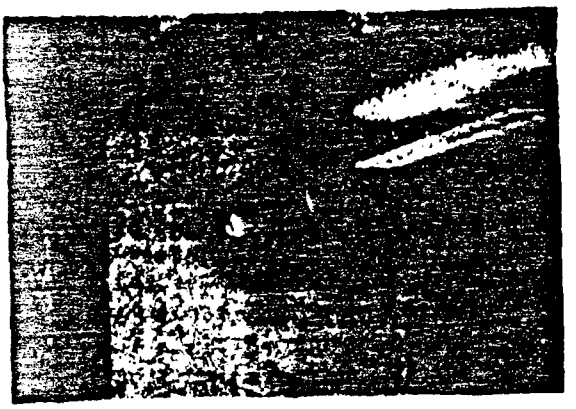
B



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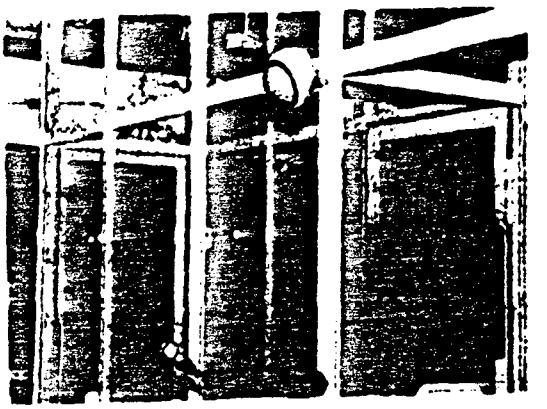
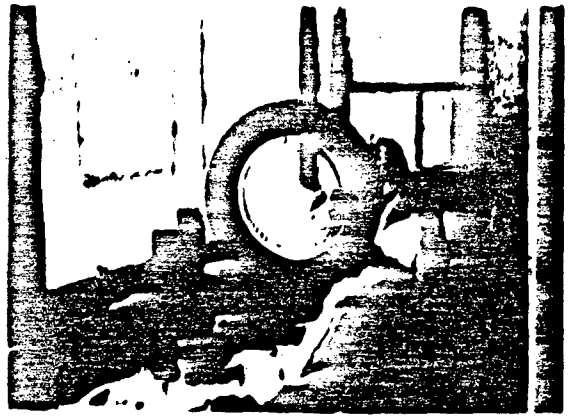


D

Figure 33. Miscellaneous Design Features.
A. Sanitary Radiator.
B. Incubator Heating Wire.
C. Overhead Facility Outlets.
D. Intercommunications System.



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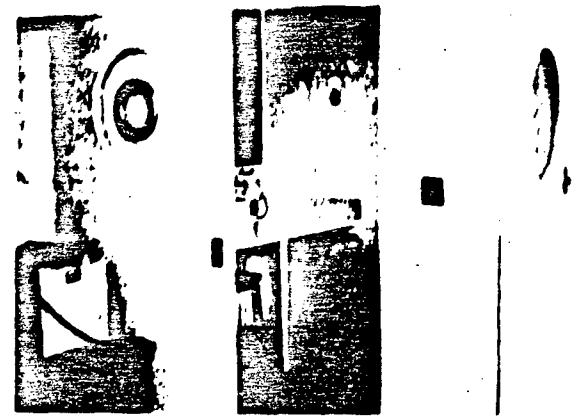

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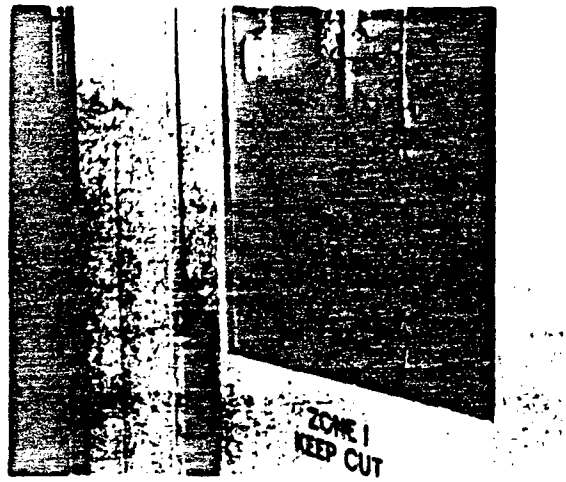

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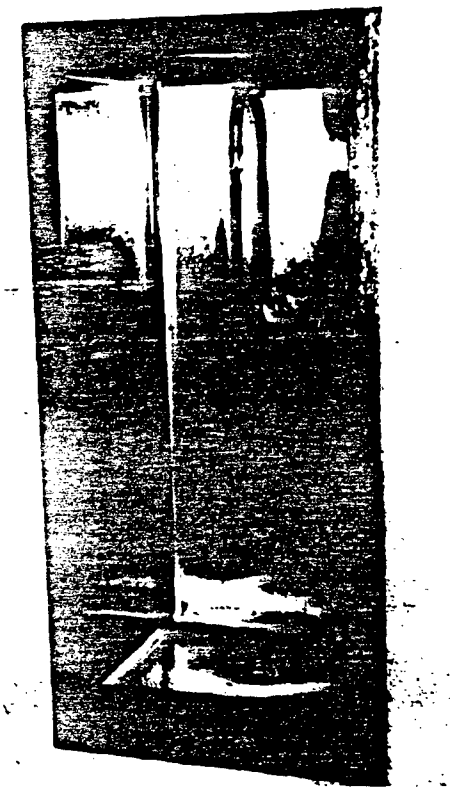
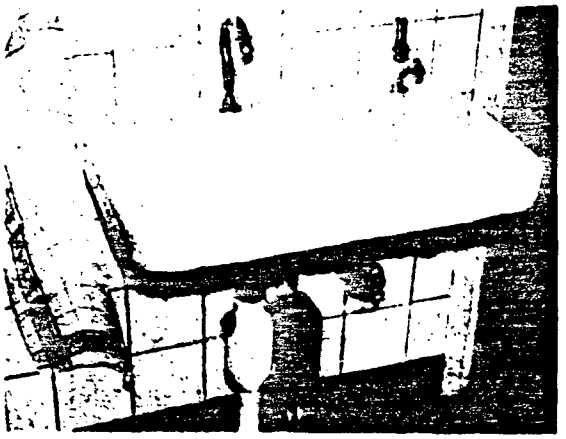


D

Figure 34. Miscellaneous Design Features.
A and B. Speaking Diaphragms.
C. Pass-Through Door.
D. Distilled Water Station.

Figure 35, E shows a rodent barrier used at one institution in a corridor between the laboratory and animal buildings. Figure 35, F shows an insect barrier. A strong current of air from a narrow slit in the ceiling prevented insects from entering the animal quarters at one institution.

A



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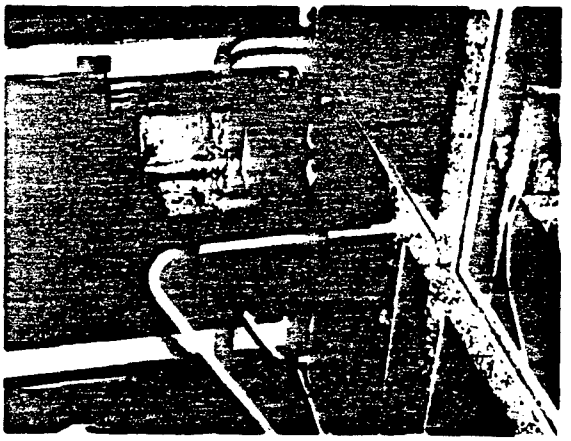
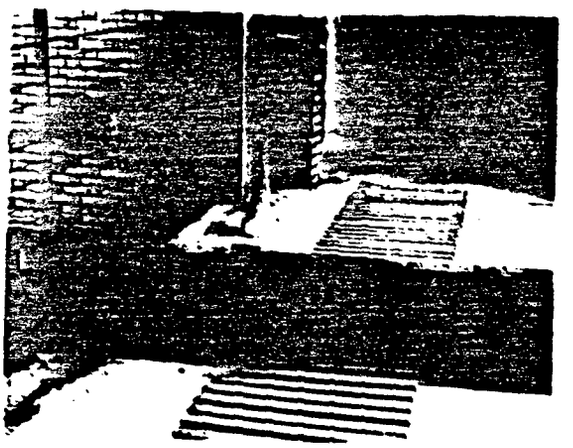


C

Figure 35. Miscellaneous Design Features.
A. Channel for Service Piping.
B and C. Foot-Operated Sinks.

D



E

F

D. Knee-Operated Soap Device.
E. Rodent Barrier.
F. Insect Barrier.

VI. LABORATORY TECHNIQUES, PROCEDURES, AND APPARATUS

A. GENERAL FINDINGS

In this chapter, fellowship findings relating to laboratory techniques and procedures will be discussed, and laboratory apparatus of special interest will be described and illustrated. Table XXXII presents a summary of some common laboratory practices.

TABLE XXXII. SUMMARY OF SOME COMMON LABORATORY PRACTICES

	PRACTICE	NUMBER OF LABORATORIES OBSERVED	PER CENT OF LABORATORIES
1.	Oral pipetting	102	62
2.	Using Pasteur pipettes	72	57
3.	Food and drinks brought into or consumed in laboratory area	102	30
4.	Smoking allowed in laboratory area	102	48
5.	Complete change of clothes required (male only)	102	10
6.	Change of shoes required	102	22
7.	White coats worn (male only)	102	90
8.	No respiratory devices used	88	66
9.	Gauze masks sometimes worn	88	32
10.	Effective type respirators used	88	2
11.	Upright, non-autoclavable pipette discard jars used	102	76

Among the obvious precautions which should be taken in laboratories handling infectious disease microorganisms are those pertaining to smoking, eating, and drinking. Yet in 30 per cent of the laboratories surveyed, food or drinks were consumed in the infectious areas. In no case was the eating of lunches involved; all instances involved the drinking of tea and coffee and the eating of cookies. Also, in 48 per cent of the institutes, smoking was allowed in the laboratories. Why greater control was not exercised over these aspects of laboratory conduct is partly explained by the observation that only rarely was there a clear separation of infectious and clean areas and only occasionally was there a suitable room which could be used for smoking and drinking.

In recent years several authors have commented on the abuses by microbiologists in the wearing of knee-length white coats — the badge of honor of the scientist. It has been pointed out, for example, that it is improper to wear the same coat in the infectious disease laboratory, the lunchroom, and the library. It has been suggested that the microbiologist fails to use his uniform according to the standards which he preaches to surgeons.[30] The author has no quarrel with these views. Among the male employees of the laboratories surveyed, 90 per cent wore white coats over their street clothes when handling infectious microorganisms. All too frequently white coats were not removed when leaving the laboratory to eat lunch or to work in a clean office. In ten per cent of the laboratories there was at least one area where a complete change of clothes was required for entrance. Female technicians in a number of laboratories wore white uniforms to work. Shoes were changed more frequently than clothing in the infectious laboratories. In Scandinavia a common custom was to provide wooden soled, clod-type scandals as shown in Figure 36.

Figure 36. Wooden Soled Laboratory Shoes.

Some information was obtained concerning the treatment of white coats and laboratory clothing worn in infectious areas. In many laboratories each person provided his own laboratory coat and made his own arrangements for laundering. In 15 laboratories, the clothing became a part of the hospital or other laundry service. No special precautions were taken in the majority of the institutes to prevent potentially contaminated laboratory clothing from leaving the building.

Even though a procedure is likely to result in infectious aerosol, a satisfactory filter respirator will prevent inhalation of air-borne organisms. But among 88 laboratories, 66 per cent used no respiratory protective devices. Thirty-two per cent used hospital-type gauze masks, which are known to offer limited protection, and only two per cent used an efficient type respirator.

To evaluate the laboratory procedures and techniques used in coping with less obvious types of hazards, a tabulation was made of the protective measures taken or the safety equipment used while carrying out eight common procedures. All procedures were not observed or discussed in all laboratories, consequently the resulting data are not entirely representative. Table XXXIII lists the procedures observed and the percentage of instances in which the protective measures employed were judged as inadequate. In most instances the inadequacy related to the possible aerosolization of the infectious microorganisms rather than contamination of surfaces.

TABLE XXXIII. EVALUATION OF PROTECTIVE MEASURES TAKEN WHILE PERFORMING EIGHT COMMON PROCEDURES

PROCEDURE	RATIO INADEQUATE PROTECTION/ TOTAL OBSERVED	PER CENT INADEQUATE
Centrifuging	64/82	78
Lyophilizing	38/43	88
Grinding and blending	52/76	68
Injecting animals	57/76	75
Autopsying animals	60/77	80
Aeration of cultures	52/57	91
Inoculation and harvesting of eggs	39/51	76
Routine diluting and plating	47/75	63

General cleanliness and orderliness of laboratory and animal rooms can be considered one measure of the adequacy of the techniques and procedures. Certainly high standards of hygiene should be maintained in infectious disease areas and particularly in those in which diagnostic procedures are undertaken or in which biologicals for human use are prepared. Failure of personnel to keep working areas reasonably free of dust and dirt, to keep materials not being used stored properly, and to separate and label potentially contaminated wastes, are indications that the proper care also may not be taken when manipulating infectious cultures. A classification of housekeeping conditions in laboratory and animal rooms is shown in Table XXXIV. In general, housekeeping in the animal quarters was poorer than in laboratory rooms.

TABLE XXXIV. EVALUATION OF HOUSEKEEPING IN 102 INFECTIOUS DISEASE LABORATORIES

CLASSIFICATION	PER CENT	
	Laboratory Rooms	Animal Rooms
Good	24	16
Fair	48	37
Poor	30	47

Twenty-four of the 102 laboratories had some method available for decontaminating entire rooms. In 11 instances formaldehyde solutions were sprayed or vaporized. Eight laboratories relied on portable ultraviolet fixtures for room decontamination, while four laboratories used mists of ethylene glycol, and one used sprays of a detergent solution.

Because a common accident in microbiological laboratories is the spillage of infectious materials following the breakage of glass dishes, flasks, or beakers, an obvious safety measure is the replacement of glass items with break resistant plastic ware. It was encouraging to note that many plastic items were being used in place of glassware in the infectious disease laboratories. Quite a few laboratories were trying disposable plastic Petri dishes, and three large laboratories were using them exclusively. A few laboratories used glass Petri dish bottoms with aluminum or ceramic covers. These are undesirable where ventilated cabinets were not used because the covers of the plates must be removed to count the bacterial colonies.

B. HAZARDOUS PROCEDURES AND TECHNIQUES

1. Case Studies

In many hazardous situations more may be involved than a mere incorrect technique or an unsafe apparatus. Often, other factors such as training, supervision, and work attitudes are involved. Because it is difficult, if not impossible, to record all such related details on tables and charts, I have prepared the following case studies to illustrate the problems encountered in infectious disease laboratories. These actual cases reveal, in many instances, the attitudes and methods of corrective action taken by the scientists in charge.

Case 1 - A well qualified M.D. started centrifuging a mouse brain suspension of a human virus. She did not use the available safety cup as required by the organization regulations. As the centrifuge reached speed she heard a tube break and shatter in the bowl. She immediately shut off the machine and opened the top of the bowl, watching the rotor come to a halt.

Then she started picking up the broken glass. A technician came in and started helping with the broken glass. The safety officer, also an M.D., came into the room at this time, found out had what had happened, ordered everyone out of the room, and placed a large sign on the door to "Keep Out." While the safety officer was in another room with the two women trying to establish what had happened, another worker ignored the sign on the door, entered the room, and started centrifuging another organism in the same centrifuge which at that time had not been decontaminated and whose bowl was still wet with the spilled virus suspension.

All nonsensitive individuals involved were given immune serum. Fortunately, no infections resulted. The laboratory director had a talk with everyone about safety procedures.

Case 2 - A laboratory technician dropped a syringe containing a culture of tubercle bacilli. It caught in the lower part of his laboratory coat but he thought that his leg had not been stuck and therefore did nothing about it. Nevertheless the man developed a tuberculoma on his upper leg and spent six months in the hospital. He has recovered and is now back to work.

Case 3 - During April one of the laboratory technicians who had been working with influenza virus developed an acute illness and died 24 hours after admission to the hospital. The illness was diagnosed as influenza. Upon investigation no known accident or unusual event was uncovered.

Case 4 - During his youth, this scientists had rheumatic fever. Eighteen years later he had a recurrence of the disease following a pipetting accident in which he had sucked a culture of staphylococci into his mouth. This made him aware of the hazards of pipetting. Now a laboratory director, this scientist will not hire nonprofessional people with a history of rheumatic fever.

Case 5 - A man who raised guinea pigs to sell to laboratories developed pulmonary tuberculosis with a strongly positive sputum. After the disease was detected, the man continued to work with his guinea pigs until about seven weeks before he was hospitalized. During this period he sold about 2000 animals. Subsequent investigation revealed that tuberculosis was detected in the "normal" guinea pigs purchased from this supplier in seven of eight different laboratories.

Case 6 - The impetus to conduct a national study on the frequency of tuberculosis infections among medical workers in one country came from a well-to-do business man. His son, a physician, contracted tuberculosis in the laboratory and died suddenly several hours after a chest X ray was taken. The father, in effect, asked the authorities what they proposed to do about such hazards to medical workers. A study was then started to collect statistical information. Eventually, recommendations were made on a national scale for reducing the laboratory risks.

Case 7 - A sixteen-year-old boy was hired to work in the dishwashing room in a laboratory in which smallpox virus was being used. It was the practice to vaccinate all department members every two years. The boy began work and was then given a note for his father to sign giving permission for the vaccination. His father refused. Several weeks elapsed before the father finally give his permission. During this time the boy continued to work. A few days after the vaccination the boy became sick and his father phoned the laboratory. The director thought it was a reaction from the vaccination. It was subsequently determined that he had a mild case of smallpox and variola virus was isolated. Investigation showed that the boy had probably become infected from contaminated glassware which he had gotten from a cart containing material to be autoclaved. The boy slept, during part of his illness, with a younger brother who developed a very severe case of smallpox. A very young child (nonvaccinated) and the mother and father (both vaccinated in childhood) escaped infection.

Obviously at least two mistakes were made which led to the infection. First, people should be vaccinated before beginning work in the laboratory. Second, it is obvious that there was not adequate separation and control of infectious and noninfectious materials. I do not believe that either of these situations had been adequately corrected. My talking with the director reminded him that he had not as yet vaccinated his new secretary!

Case 8 - A well-known scientist has been in charge of a smallpox vaccine laboratory for ten years during which time there has been only one known occupational illness. He forgot to immunize a new man who went to work in the vaccine production unit. The employee developed a lesion on his forearm where his arm had touched the inoculated abdomen of a cow.

Case 9 - Severe allergic reactions were experienced by a scientist in the laboratory. Each incident was preceeded by the carrying out of a technique which involved the centrifugation of dead tuberculosis organisms. After it happened about three times, the laboratory director realized it was from breathing aerosols created during the centrifuging operation. A cabinet was designed for the centrifuge. The director told me that some of the things he has his people do are only window dressing (e.g. wearing of gauze masks) but are required by the university for insurance purposes.

Case 10 - Professor X, who is aware of many of the hazards of infectious laboratory work, took charge of an institutional laboratory about a year ago. At that time he advised the university authorities that he would not be responsible for the health of his people unless he was provided with better facilities. Consequently, a new building has been approved and plans will be begun soon. Because he does not expect the new building to be finished for several years, the professor also notified the authorities that the following restrictions were to be imposed on the diagnostic functions:

(a) No tuberculosis sensitivity or resistance tests will be done.
(b) No virus animal work will be done.
(c) No work with Coxsackie viruses will be done.
(d) No other highly infectious viruses or bacteria will be handled.

Case 11 - Several years ago an investigator initiated a research project using aerosols of tubercle bacilli. He promptly acquired a respiratory infection, the research project was dropped, and has not been restarted.

Case 12 - A scientist interested in safe laboratory procedures was visiting a neighboring laboratory and happened to observe what he considered to be an unsafe procedure. He pointed out the hazard to the director as they walked through the laboratory. The director was upset and told him he should not make such careless remarks in front of the technicians. The director and the visitor, who were friends, made a bet on whether or not the procedure produced a hazard. The visitor devised a simple sampling apparatus and asked the same technician to repeat the procedure using a tracer organism. The recovery of air-borne organisms during the experiment convinced the laboratory director and the technician. Appropriate changes in the technique were subsequently made.

Case 13 - Several years ago, a university professor gave one of his technicians an old, dried-up slant culture of Bacillus anthracis and told him to try to recover viable organisms. Several days later in looking at some colonies of another organism on blood agar he noticed typical anthrax colonies outside the streaked area of the plate. (These had not been recognized by the technician.) Mouse injection proved the contaminant to be B. anthracis. Investigation revealed that when the technician had been given the old anthrax culture he had filled the test tube to the brim with broth and then mixed with an inoculating loop. The hollow metal handle of the inoculating loop had taken up some of the contaminated fluid. Subsequently, when the loop was heated, the fluid in the handle became hot and sprayed out, contaminating the air and the plate being streaked. Following this accident, the professor went to the dean and told him he could not be responsible for the health of his people unless ultraviolet lamps were placed in the laboratories.

Case 14 - Sputum specimens were being processed by the acid digestion method for recovery of tubercle bacilli. Acid had been spilled into the brass centrifuge cups and a hole had corroded through the bottom of one of them. While the centrifuge was in operation a glass tube containing a specimen broke, and the hole in the brass cup allowed the culture to spray into the room. Two persons who were in the room at that time received massive respiratory infections.

Case 15 - Several years ago there was a fatality from a herpes virus infection. A woman who had been harvesting eggs inoculated with herpes virus developed a typical blister in one nostril. She went into a coma and died of a virus encephalitis. The virus was not isolated but the laboratory director is positive that it was a laboratory infection.

Case 16. A woman scientist had a very serious infection with St. Louis encephalitis virus several years ago and almost died. She was preparing live antigens. In the same virus laboratory (about six years ago) all five persons in the psittacosis laboratory became infected. One person was infected three times, and the cleaning woman also got psittacosis. All people were treated with Aureomycin.

Case 17 - A virologist was injecting an animal with cowpox virus when the needle came off of the syringe and the culture sprayed into his right eye. A severe infection followed which left him with impaired vision in that eye. During his one-month hospitalization, the virus was twice isolated from the eye. The isolates were indistinguishable from the original strain.

When working with Russian spring-summer encephalitis virus, the same person has twice accidently inoculated himself. He was ill for a short while after one such accident and he now has a significant serum titer. Ten other persons are involved in work with this virus (five directly) but no titers have been taken. They may have all had inapparent infections.

Case 18 - Early on the day of my visit I asked the laboratory director if there had been any laboratory illnesses among workers at the institute. He replied that as long as he had been there he recalled only two laboratory infections. These occurred between 1920 and 1930. One was a syphilitic infection of the finger resulting from a self-inoculation. The other was a case of diphtheria following aspiration of a culture through a pipette.

We discussed these cases for several minutes. Then the assistant director spoke up and said, "Oh yes, we have had two cases of brucellosis in the last two years." The causes were not determined.

Then the director said that he had forgotten about the laboratory epidemic in 1947 in which there were 15 cases of Q fever among workers throughout the building. Recovery was satisfactory in all cases except for the director himself who, following the infection, suffered from pulmonary impairment for three years. No investigation of the Q fever infections was conducted. The worker who everyone thought was responsible left a short time later. The director and his assistant stated that the laboratory man was a "sloppy worker" and that they assumed that he had been centrifuging or grinding tissue.

I next asked the director (this was still in the morning) if there had been any tuberculosis infections. He replied that there had been no infections and that most operations with tubercle bacilli were relatively safe. At that point the conversation turned to technical aspects of his research with tubercle bacilli.

In the afternoon, after my lecture, the conversation turned to safe means of challenging animals with infectious aerosols. This conversation prompted the director to remember that there had been some tuberculosis infections. In fact there had been five infections resulting in two fatalities. One of the cases was the director's wife who had an eye infection and today, as a result, has impaired vision in that eye. Three of the five cases brought suit and were awarded compensation payments (it wasn't clear if the institute or the government paid the compensation). Apparently the infections resulted from experiments in which guinea pigs were being exposed in a crude device to aerosols of tubercle bacilli. No specific investigation was conducted.

To sum up, at first I was told that there had been only two laboratory infections, but before the day was over I had noted 24 infections in my notebook.

1 - Syphilis
1 - Diphtheria
2 - Brucellosis
15 - Q fever
5 - Tuberculosis

Many laboratory directors do not enjoy thinking or talking about their occupational illnesses. I was fortunate enough to win the confidence of some directors and have been told of their past experiences. Even then, however, I have the feeling that directors seldom, if ever, discuss laboratory infections with their staff or with others. Laboratory infections are sometimes skeletons in the closet which are not to be taken out. Few laboratory directors keep written records of laboratory infections.

Case 19 - The laboratory director avoided telling me of any laboratory infections as did the other staff members. But Dr. Y, with whom I became friendly, told me that there had been six cases of brucellosis in the department but none in the last three years. The technician presently working with Dr. Y (a refugee from East Germany) has been working with brucella cultures for three years without becoming infected. Dr. Y stated that his technician washes her hands at least 30 times a day. His former technician contracted brucellosis after working in the laboratory for six months. She almost never washed her hands. I could not find out what happened to the persons who became infected but it was obvious that technicians with brucellosis were encouraged to leave.

Case 20 - Although the laboratory director and his staff seemed pleased to talk to me and to show me the institute, they displayed little or no interest in microbiological safety insofar as their own institute was concerned. This seemed strange to me because it was apparent that laboratory infections were a problem. As a matter of fact six weeks prior to my visit there had been four cases of psittacosis among a group of laboratory workers who act as a clean-up crew. (Presumably there are only four members of the crew.) These workers had handled infected birds, (two workers had transported some live infected birds in an automobile) cleaned up patients' rooms, and decontaminated laboratory and hospital items. They wore hospital gauze masks during all procedures. The director feels that the gauze masks are the only protection required during work with respiratory pathogens. This seemed to be the only precautionary measure used in the infectious disease laboratories. The director felt that two of the workers may have been infected in the automobile but he does not know how the others became infected. Prior to these infections there were two other cases of psittacosis among laboratory workers.

Psittacosis among the population of this city is a yearly problem. By law, parakeets may not be imported for domestic sale but every year before Christmas there is lively smuggling and black market activity. The institute expects the human cases to begin in January and February. Although the laboratory director is aware of the fact that his laboratory workers will be exposed to the infectious risks of psittacosis every year, no action is taken.

In 1946 there was an epidemic of Q fever in this institute in which a total of 60 persons, including the director, were infected. Antibiotics were not immediately available and some of the illnesses were severe. Not only were laboratory people and doctors infected, but also construction workers in the building and visitors. The director stated that he believed that the use of a low speed centrifuge was responsible but that no investigation was made. The institute no longer prepares Q fever antigen.

Case 21 - The director stated that four types of accidents occur in his laboratory:

1. Oral aspiration of infectious fluid through a pipette. This was the most frequent and had been the cause of four infections (not included in the tabulation in Chapter II).
2. Dropping or spilling infectious cultures on the floor.
3. Cuts and scratches becoming contaminated with infectious cultures.
4. Self-inoculation with syringe and needle.

He further stated that his safety program consisted of telling his people (about 10 to 15) that they must report immediately to him for antibiotic treatment if they have one of the above accidents. He warns them that they may get into trouble if they do not report promptly. Obviously this is not an accident prevention program but a medical treatment service.

Case 22 - Dr. Z is aware that, as the laboratory director, he has a direct concern with problems of laboratory safety. He stated, however, that he was reluctant to be forceful in interfering with the way in which his subordinates operate their laboratories. In one laboratory there is a woman technician who has had five laboratory infections — "she gets infected with everything she works with." The director feels that she is a sloppy technician and that she should not be allowed to work with pathogens. Yet he had taken no action and leaves it entirely in the hands of the specific laboratory chief (who also has taken no action).

2. List of Typical Hazardous Procedures

In addition to the above case studies, a listing was made of the types of hazardous procedures observed during the study. This list includes some of the procedures frequently seen as well as some that were encountered only once or twice. While many will be discussed later in detail, this presentation will serve to illustrate the variety of techniques and procedures observed which were considered to create conditions for potential infection of laboratory personnel.

a. Oral pipetting of infectious cultures and blowing out the last drop from a pipette.
b. Using an electric fan in an infectious animal room and autopsy room.
c. Leaving dissected, infected guinea pigs on the bench top over the lunch hour.
d. Disinfecting animal carcasses by boiling.
e. Cleaning a contaminated laboratory sewage holding tank.
f. "Killing" anthrax spores by boiling for 10 minutes.
g. Blowing unfiltered air from a variola virus laboratory toward an adjacent building where smallpox vaccine is produced.
h. Handling contaminated pipettes before they are autoclaved.
i. Failure to use needle-locking syringes when working with infectious cultures.
j. Failure to wrap a vial of lyophilized culture with disinfectant soaked cotton before breaking.
k. Using coiled metal wires for transferring infectious liquids.
l. Handling potentially infectious blood specimens without gloves.
m. Not filtering the exhaust air from lyophilizing apparatus. Failure to sterilize the apparatus after use with pathogens.
n. Shaking tubercle bacilli specimens without placing them in aerosol-tight containers.
o. Harvesting spinal cords from infected suckling mice by water pressure from a syringe.
p. Allowing children to come into the infectious disease laboratory.
q. Producing BCG vaccine in a building which also houses a laboratory handling virulent tubercle bacilli.
r. Re-using contaminated cardboard egg trays without sterilizing them.

s. Allowing mice to escape in an infectious disease animal room.
t. Failure to enclose Sharples or DeLaval centrifuges used with live cultures.
u. Failure to use ventilated cabinets to enclose hazardous laboratory manipulations.

C. AEROBIOLOGICAL RESEARCH CHAMBERS AND PROCEDURES

In the medical research institutions visited there was surprisingly little attention being given to quantitative experiments with aerosols of respiratory disease agents. This, however, is not an indication of lack of interest. Respiratory diseases, particularly viral diseases and tuberculosis, receive a great deal of research attention, but aerobiological experiments are seldom done because of the safety, technological, and financial difficulties. Many scientists use the classical methods of intranasal and intratracheal inoculation for infection of animals. Several investigators used animal cross-infection processes to create respiratory infections in experimental animals.

Some type of chamber or apparatus for exposure of laboratory animals to aerosols of respiratory pathogens was used in 11 of the 102 laboratories. Four of the 11 were U.S. laboratories. These are shown in Figure 37.

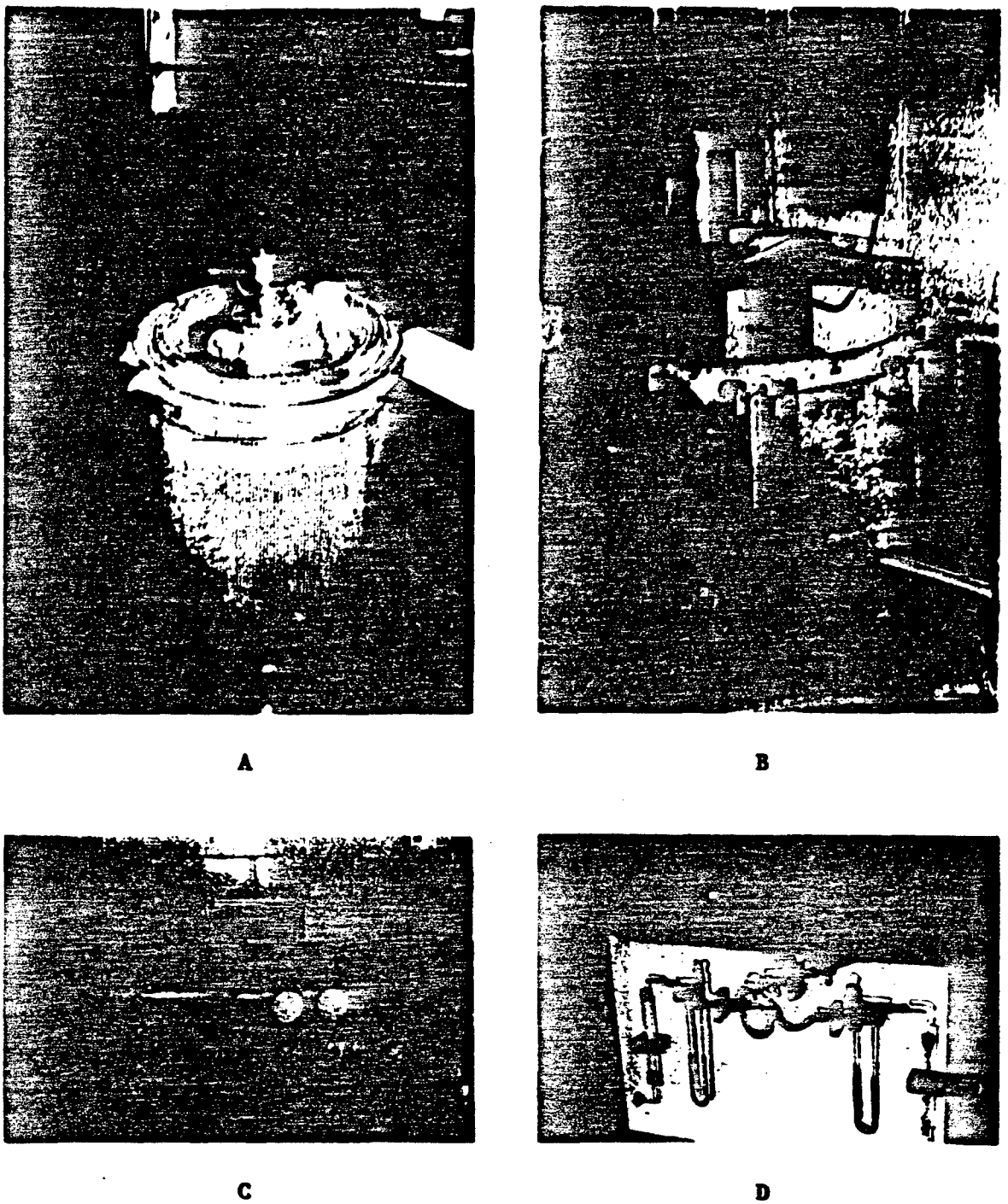
Figure 37, A shows a crude chamber for the exposure of mice made from a desiccator. Air entering through the tube in the top operates a small nebulizer inside. Such a chamber is entirely inadequate for experiments with human pathogens. Figure 37, B is the chamber used by Dr. Max Lurie at Phipps Institute for the exposure of animals to aerosols of tubercle bacilli. The top is of Plexiglas. The chamber is decontaminated with an ultraviolet lamp inside the chamber. The usual aerosol exposure time for animals is 30 minutes.

Figure 37, C is a Henderson Aerosol Exposure Apparatus owned by the U.S. Army Biological Laboratories in use in a university laboratory. It was developed in England by Dr. D. W. Henderson[31] and further developed at the Biological Laboratories. The apparatus is placed in a ventilated cabinet when used with human pathogens. The Henderson Apparatus provided a greater degree of personnel protection than any of the other devices seen in U.S. laboratories.

Figure 37, D is an aerosol exposure chamber developed and used by Dr. Gardner Middlebrook at the National Jewish Hospital laboratories in Denver.[32] A flow diagram of the apparatus is shown in Figure 38. Further details of the apparatus are as follows:

Cabinet - A wooden box, approximately 28 inches wide by 31 inches long by 18 inches high, with hinged door to protect glassware.

Tank - A spun aluminum tank, 24 inches in diameter and 14 inches deep.



A B C D

Figure 37. Aerosol Chambers.
A. Desiccator Chamber.
B. Lurie Chamber.
C. Henderson Apparatus.
D. Middlebrook Apparatus.

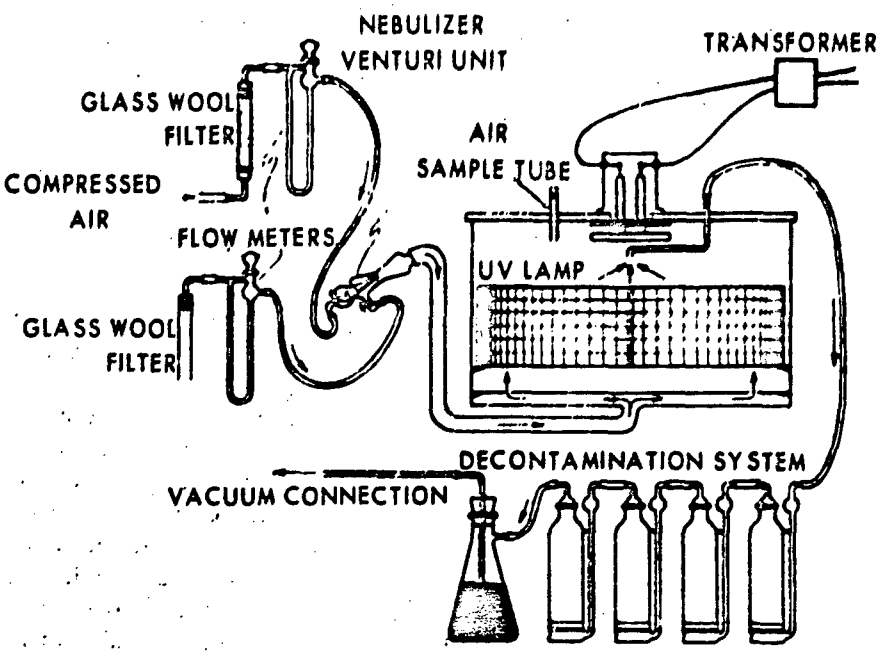


Figure 38. Flow Diagram of the Middlebrook Air-Borne Infection Apparatus.

Cage - Removable stainless steel mesh basket-cage with five compartments and rotatable lid. Five groups of mice, (of up to 20 each), can be kept separated and can be introduced and removed through a port in the top.

Top - Plexiglas top secured with 12 radial clamps. 30-watt, high intensity, circular quartz glass ultraviolet lamp mounted to lid. Two openings provided; one hose connection to decontamination system and one to permit removal of air samples to be tested for content of droplet nuclei. To prevent accidental cracking of the large lid by a vacuum build-up, an air flow safety gage is mounted to the lid. Excessive vacuum will open a valve in the gage.

Glassware - Two glass-wool air filters, two all-glass monometric type flow meters for measurement of air flow and a nebulizer-venturi unit. This nebulizer-venturi unit is designed so that air under pressure is forced into the nebulizer, nebulizes the suspension therein, mixes with controllable amount of room air and is drawn into the tank by the vacuum system.

This exposure apparatus is commercially available from Tri-R Instruments, 144-13 Jamaica Avenue, Jamaica 35, New York, at a cost of $900.00.

D. ANIMAL CARE

Animals are an important part of many infectious laboratory operations. The type of animal that is raised or procured, how it is handled and cared for, what type of housing facilities are provided, and how the sacrifice, autopsy, and subsequent disposal is carried out are factors which influence the reliability of the laboratory data obtained as well as the well-being and safety of persons handling animals.

The general quality of animal care was very poor in many laboratories. The study techniques used provided no quantitative basis for comparing various laboratories, but a variety of general observations were made.

When comparing the general level of animal care in this country with that of foreign countries it would appear that the competence of the foreign laboratory animal handler is superior. This is particularly true in England where animal technicians are trained and must pass qualifying examinations. In the U.S., however, there was ample evidence that increased attention is being paid to the qualifications of individuals hired to care for laboratory animals. For example, the larger laboratories at universities and pharmaceutical firms frequently have centralized all animal care and procurement and placed a qualified veterinarian in direct charge of the "vivarium."

There is little doubt, in my opinion, that the quality of the laboratory animals used in infectious disease laboratories in the U.S. was superior to that of the foreign countries visited. However, in England, the activities of the Laboratory Animals Centre are making an impact on the quality of the laboratory animals raised in that country. Dr. W. Lane-Petter, the director, is also the Secretary-General of the International Committee on Laboratory Animals (ICLA). The committee was organized in 1956 under the auspices of the International Union of Biological Sciences and the Council for International Organizations of Medical Sciences, with the assistance of UNESCO. The ICLA certainly has a fertile field in which to work and, partly through the participation by the Laboratory Animals Centre, much useful work is being done to improve the quality of laboratory animals and their care. The Centre has sponsored a number of useful publications in the laboratory animal field.

In the U.S. laboratories, facilities for housing both normal and infected laboratory animals were generally better than in the other countries visited. Fortunately the need for better animal quarters, improved sanitation in animal houses, etc., is beginning to be recognized, and improvement of present animal quarters was being planned by many laboratories. Little information was available on the design of rooms to house infected animals. Also, some of the recommendations are obviously rather conservative when one considers the many engineering techniques which have been developed to improve hygiene and to provide environmental control.

In many institutions the lack of money is the greatest deterrent to improved animal care. The extreme was seen in one country where several laboratories apparently used no animals because of their high cost. In other laboratories it was not uncommon to find that the animal room was a converted coal cellar, a shed attached to the back of the building, or a former horse stable. Some of the more modern animal quarters are discussed in Chapter V.

Although germ-free animal laboratories were inspected in Japan and Sweden, only one foreign laboratory visited was active in the production of specific-pathogen-free (SPF) animals. Production of SPF rats and mice began at the Imperial Chemicals Industries, Ltd., laboratories during 1960 on a scale sufficient to supply all of the demands of the research units.

Animals were used in 92 of the 102 laboratories (90 per cent). In 33 laboratories normal and infected animals were held in separate buildings. Housekeeping in 47 per cent of the animal quarters was judged as poor. Only 16 per cent of the animal quarters appeared to be kept acceptably clean. Furthermore, in my opinion, in only four per cent of the laboratories were the animal holding facilities sufficient to prevent cross-infection of animals or infection of animal workers. It is fortunate that in most laboratories infectious animal operations were done on a relatively small scale. In 38 per cent of the laboratories known instances on animal cross infection were mentioned. Only 18 per cent of the laboratories had any type of special equipment for handling infected animals.

Autoclaves were located within the animal quarters in only 27 laboratories. In an additional 47 laboratories autoclaves were available elsewhere in the building. In 67 per cent of the animal facilities, infectious animal cages were not autoclaved.

In almost all laboratories (98 per cent) infected dead animals were autoclaved or incinerated:

Autoclaved	- 21 per cent
Incinerated	- 42 per cent
Autoclaved and Incinerated	- 35 per cent

Autopsy rooms were, in general, better equipped than animal holding rooms. However, only 11 of 89 rooms were considered to be adequately equipped and properly used.

Monkeys were used in 42 per cent of those laboratories where animals were employed. These were exclusively for virus operations and most were used to supply kidney tissue or for safety testing of poliomyelitis vaccines. In 34 per cent of the laboratories using monkeys, the animals were not tuberculin tested. Most laboratory directors (74 per cent) expressed some concern about possible B-virus infections. Three laboratories had had B- virus infections among their workers.

The apparatus used by Perkins and Short[33] in England for sterilizing animal rooms, racks, and cage is shown schematically in Figure 39. Tego, M.H.G., a German-made bactericide, is used in a one per cent solution in hot water at 40° to 60°C. It is an amphoteric surface-active agent [dodecyl-di (amino-ethyl) - glycine-hydrochloride] supplied in concentrated liquid form and reported to combine the bactericidal properties of the cationic chemicals with the detergent properties of the anionic compounds. For the treatment of animal cages the above authors found it necessary to soak the cages in hot one per cent Tego solution. The solution was allowed to dry on the cages and this, it was felt, provided a bactericidal film which made subsequent chemical sterilization easier.

Animal room equipment is discussed in Chapter VII.

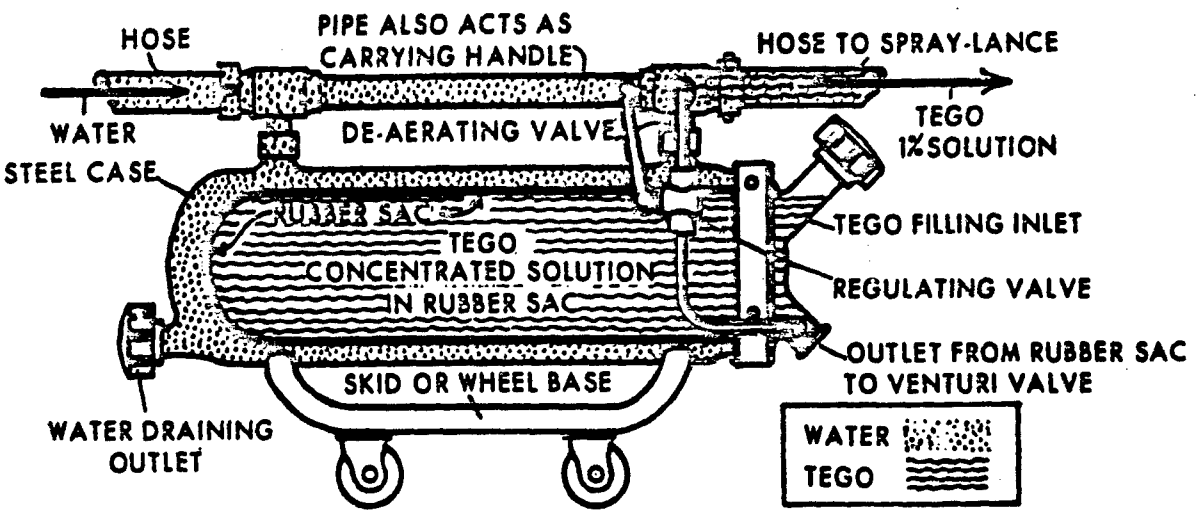


Figure 39. Tego Mixing Apparatus.

E. AUTOCLAVES AND HEAT STERILIZATION TECHNIQUES

In many laboratories the devices used for sterilizing materials with steam under pressure were inadequate in design and number.

Twenty-seven per cent of the laboratories used one or more top-loading autoclaves. Several of these old-style devices which are still in use are shown in Figure 40. As a general rule the top-loading autoclaves did not have a means of exhausting air or a thermometer to indicate the internal chamber temperature. It was rather disheartening to find that directors of several newly built laboratories had purchased new top-loading autoclaves for their buildings. These are shown in Figure 41. Top-loading autoclaves were not seen in U.S. laboratories, but they are very

much in use in Europe and Australia. Because of its simpler design, top-loading autoclaves are cheaper than horizontal ones. Most are operated by gas or electricity. No top loading autoclaves were seen which served hospital needs. Apart from the difficulties in obtaining proper internal sterilizing temperatures, top loading autoclaves have several undesirable safety features. There is, for example, a distinct burn hazard created when personnel bend over the uninsulated vessels to load or unload materials. Loading generally requires the use of special wire trays. This means that contaminated materials to be sterilized often must be handled or moved from one type of container to another. To illustrate, a flat pipette discard tray will not fit into most top loading autoclaves and it is necessary to transfer the pipettes to another container before treatment. Undoubtedly the general inconvenience of using these autoclaves discourages their use in sterilizing some contaminated materials.

In England and Scotland the inadequacies of autoclaving devices have been realized and several scientists, particularly Professor Robert Knox at Guy's Hospital Medical School and Professor J. W. Howie of the University of Glasgow, have been active in research sponsored by the Medical Research Council to improve steam sterilization methods in Britain.[34-36] An effort is being made by this group to encourage the use of rapid, high vacuum evacuation of autoclaves used in hospitals. Of particular importance is a recent publication[37] which shows how rapid high vacuum can be used to decrease sterilization time and increase penetration of steam into materials being autoclaved.

A serious problem facing many laboratories was an inadequate number of autoclaves and the frequent practice of locating all autoclaves for a laboratory building in one central area. This problem was more typical of foreign rather than U.S. laboratories. The practical consequence of an inadequate number of sterilizing devices is that some contaminated materials may be treated by alternate but less desirable methods or not treated at all. As an example, in only one third of the laboratories were infectious animal cages sterilized before re-use. And when they were sterilized, the cage debris was frequently removed first; an action contrary to good safety practice. The theoretical requirements for locating autoclaves in infectious disease laboratories may be stated as follows:

1. The distance between the contamination source (the laboratory or animal room) and the sterilizing device should be as short as possible. Preferably the autoclave should be located in or immediately adjacent to the room.

2. If contaminated materials must be carried to an autoclave some distance away, they should be put in closed containers to avoid spilling and dropping. Furthermore it should not be necessary to transport contaminated materials through a clean area.

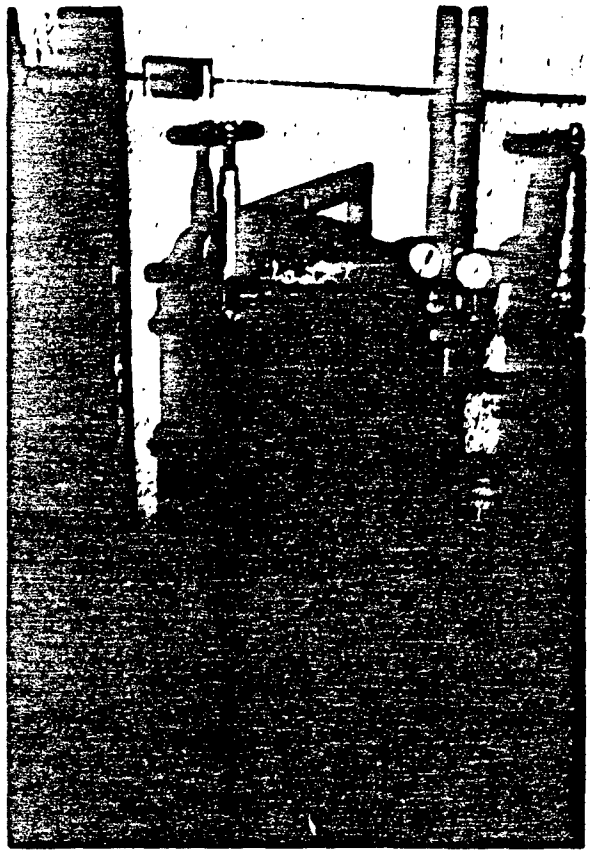


Figure 40. Old Top-Loading Autoclaves.

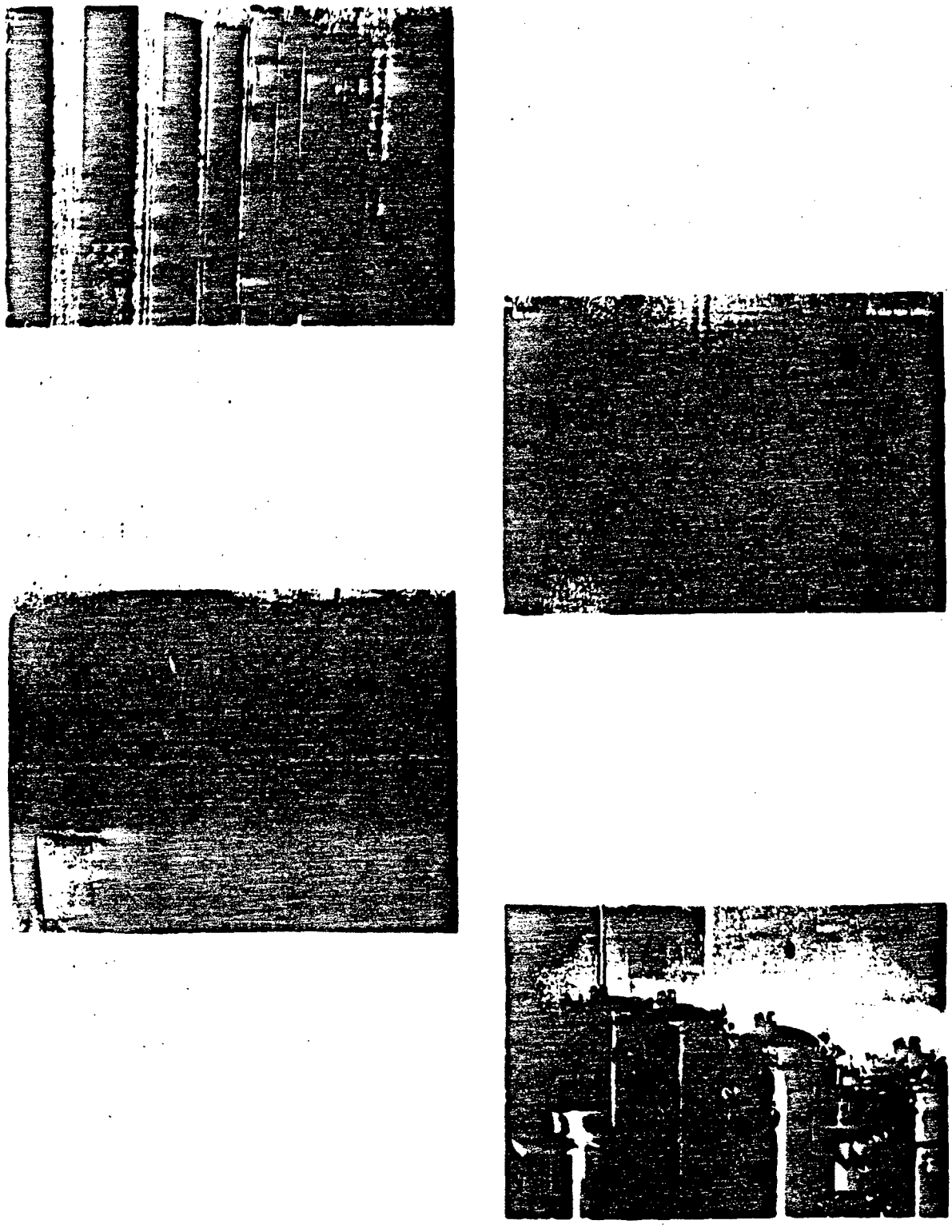


Figure 41. New Top-Loading Autoclaves.

3. Unless there is an adequate system to avoid mix-up, for example the use of a through-the-wall, double-doored autoclave, the device used to sterilize discard materials should be separate from that used to sterilize media, pharmacological preparations, hospital bandages, and other noninfectious materials.

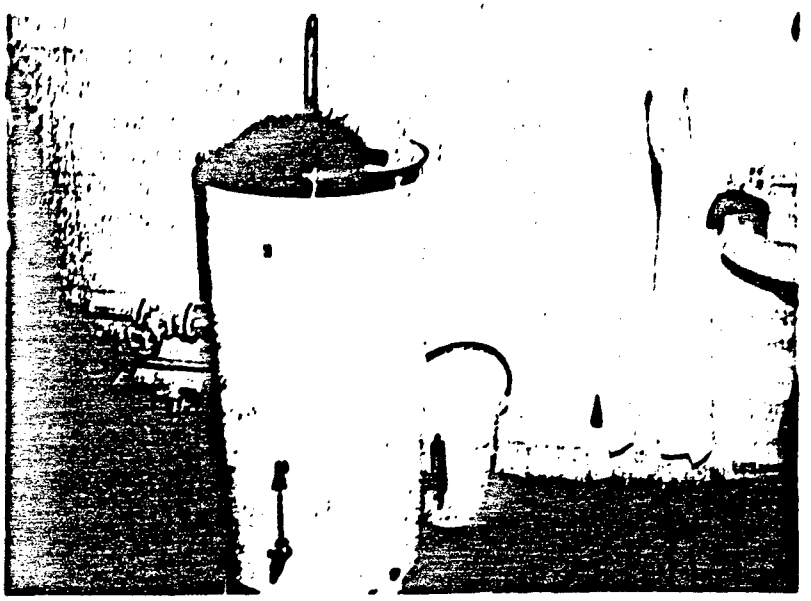
Unfortunately these requirements were frequently violated. The most commonly observed situation was the use of a single room for the sterilization of contaminated discard materials, dishwashing, and preparation of sterile solutions, instruments, and media. Where this situation exists, in my opinion, sooner or later a non-autoclaved flask or test tube of culture will be poured into the dishwashing sink and the personnel will be exposed to this hazard. Surveys of laboratory infections include enough cases among laboratory cleaning personnel to substantiate this view. Furthermore it is obvious that, in general, the type of person working in the dishwashing-media preparation room is less able to evaluate the infectious hazards of his activities than are the professional personnel and the technicians.

In some laboratories realization of these hazards had resulted in alternate means of assuring that materials leaving the laboratories had been decontaminated. In several laboratories, contaminated materials were put in a pail of water and boiled over a flame before delivery to the dishwashing room. In other institutions dry heat ovens, called "killing incubators," were placed in each infectious disease laboratory and maintained at about 60°C. Discard material was placed in the incubators overnight before being removed from the room. When nonspore agents were used this seemed to be an effective method of reducing hazards to dishwashing personnel. The disadvantages are that some materials cannot be exposed to dry heat and that used glassware removed from the incubators is difficult to clean because media and culture material have been baked on.

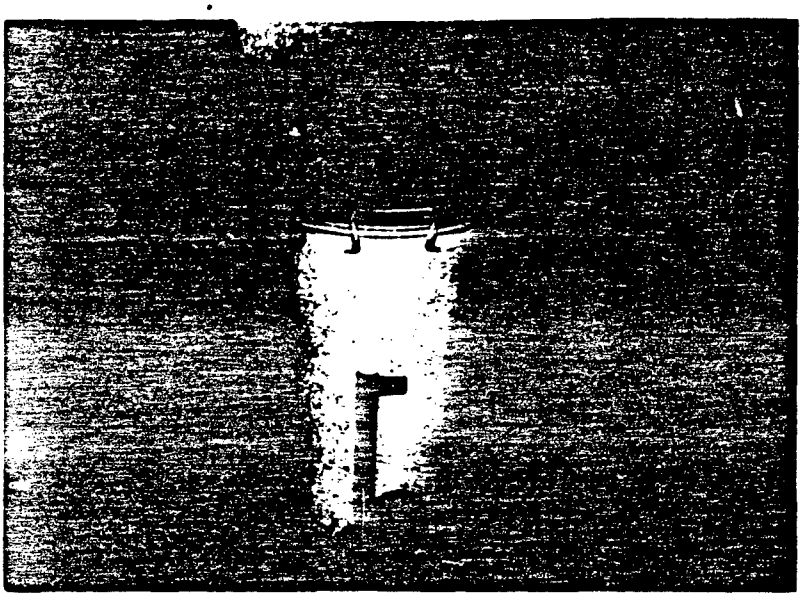
In one foreign virus laboratory where there had been difficulty with cross-contamination of strains of poliomyelitis, each laboratory was equipped with a nonpressure steaming vessel for the daily treatment of the white coats worn in the laboratory (Figure 42,A).

At the State Bacteriological and Public Health Institution in Munich, Germany, Professor Freytag, the director, had developed a small portable top-loading autoclave which is available commercially in that country and is being used by the German Army for field sterilization of hospital instruments and bandages.[38] This apparatus, shown in Figure 42, B, looks like a pressure cooker and contains water to produce steam. Materials to be sterilized are loaded in such a manner that air in the chamber is removed as steam is generated by heat from any external source.

A number of laboratories used alternate means of sterilizing infected animal cages. A common method was to emerse the cages in a large vat of boiling water. This, however, required that the infectious bedding and



A



B

Figure 42. Apparatus for Sterilizing Laboratory Clothing.
A. Steaming Vessel for Laboratory Clothing.
B. Portable Field Autoclave.

debris in each cage be removed before boiling. With certain infectious agents the hazard of this operation is obvious since infected animals excrete the microorganisms in their feces and urine. It should be mentioned that in laboratories where large numbers of animals were handled it was obvious that many more autoclaves would have been necessary to sterilize all infectious animal cages. One outstanding need, therefore, is for a cheaper and more convenient method of sterilizing animal cages without removing the infectious bedding.

Another alternate to steam sterilization of cages is that developed by Perkins and Short[33] and described on page 152. An amphoteric detergent is mixed with hot water and sprayed under pressure. But this method also requires initial removal of the contaminated cage bedding. Various types of steam generating devices were also used for disinfecting and cleaning animal cages but these had essentially the same disadvantages. Other types of autoclaves in use in European laboratories are shown in Figure 43.

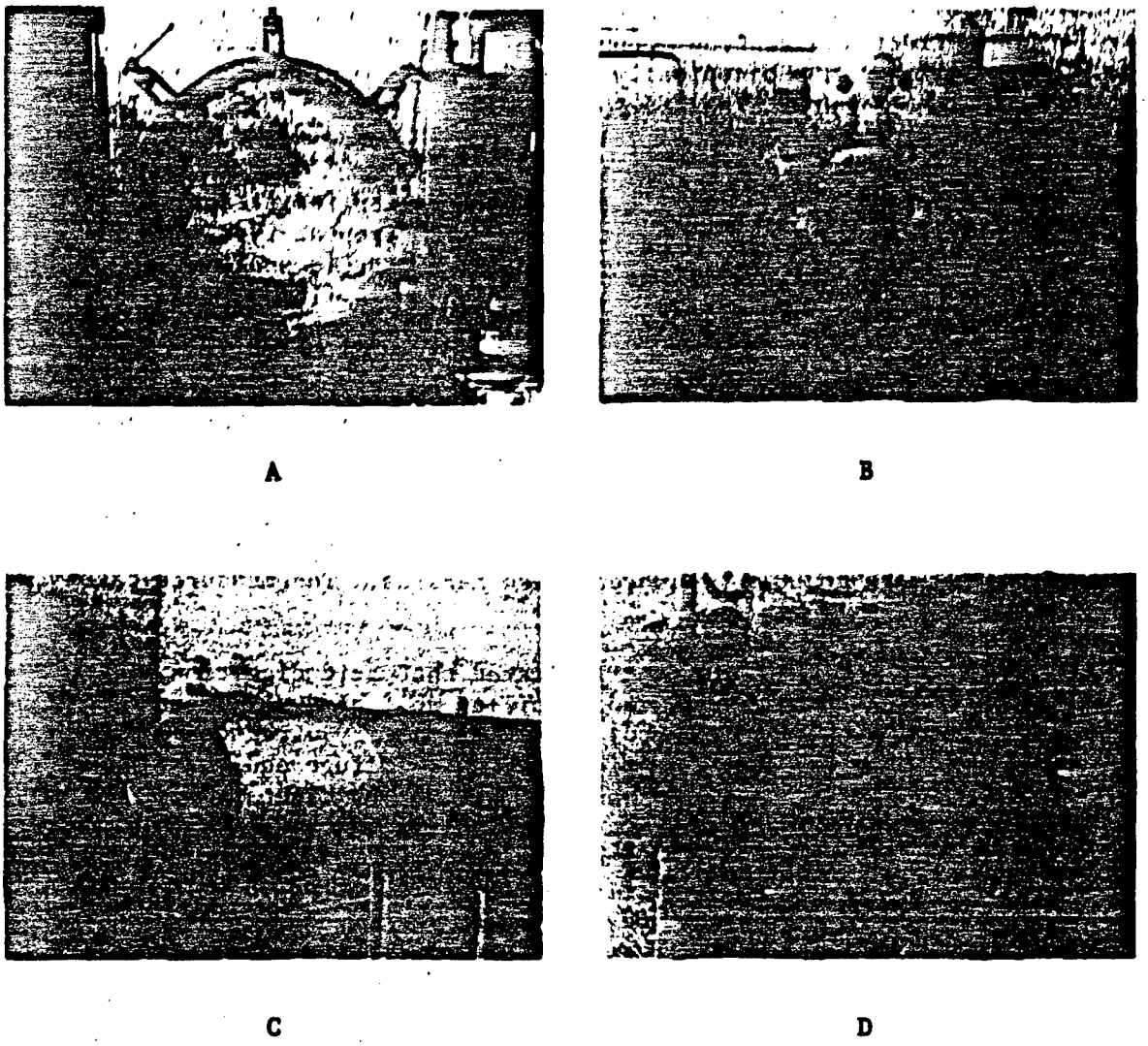
F. CENTRIFUGE PROCEDURES AND APPARATUS

An observation made by three workers in a tuberculosis laboratory in Liverpool, England, prompted them to study the hazards connected with the use of their angle-head centrifuge. Whitwell, Taylor, and Oliver[39] observed that the laboratory wall behind their centrifuge was marked with dirty horizontal streaks. The centrifuge was used daily for concentrating sputum from suspected tuberculosis patients.

Using several test organisms, as well as chemical detection methods, these authors determined that a spray of fine droplets was produced when the centrifuge was operated. Subsequent investigation revealed the cause. Screw-capped tubes were used in the centrifuge. Uncapping and recapping of the tubes before centrifugation, during intermediate steps, or during shaking contaminated the rims and trapped fluid between the threads of the tube and the cap. Centrifugation of these tubes threw out the fluid and produced an aerosol which escaped from the angle head whose top and bearings were not aerosol tight.

These studies also revealed that no aerosol was produced if uncapping procedures were eliminated. If this is impracticable, each time a centrifuge tube is opened it should be flamed and provided with a sterile screw-cap before recentrifuging.

A subsequent British committee report dealing with tuberculosis laboratory precautions[40] made recommendations regarding the use of centrifuges. The committee pointed out the desirability of developing sputum culture methods which would eliminate centrifuging. One method was based on the report that tubercle bacilli in microscopically-positive sputa which has been digested with sodium hydroxide can be recovered culturely as easily as from samples which have also been neutralized and centrifuged. This suggested that the centrifuging step might be eliminated. Alternately, if



A B C D

Figure 43. European Autoclaves.
A. Typical, Larger Sized European Sterilizers Which Close by Means of Eight or More Lug Clamps.
B. German-Made Electric Autoclave with Multiple Closing Clamps.
C. American-Made Electric Autoclaves Which Were Installed in a Greek Hospital Laboratory by the U.S. Army.
D. A Modern Double-Doored, Automatic Type Autoclave in a German Virus Laboratory. Note that the autoclave door hinges on the left.

the results of microscopic examination are known before the digestion procedure, the direct inoculation technique evaluated by O'Hea[41] will eliminate centrifuging. Microscopically negative sputa would still require the centrifuging step, but the hazard should be less owing to the smaller numbers of tubercle bacilli.

In view of the hazards associated with the centrifuging screw-capped bottles in angle-head centrifuges (e.g.: In a horizontal-type centrifuge liquid escaping from the screw-cap runs down the bottle and into the trunnion cup, but in an angle head the liquid may be flung horizontally into the air.) and because of the likelihood that centrifuge tubes will be overfilled, the committee felt that the use of angle-head centrifuges should be avoided in the tuberculosis laboratory. It was suggested that trunnion cups be balanced with a 50 per cent solution of methyl alcohol and that they be sterilized after use.

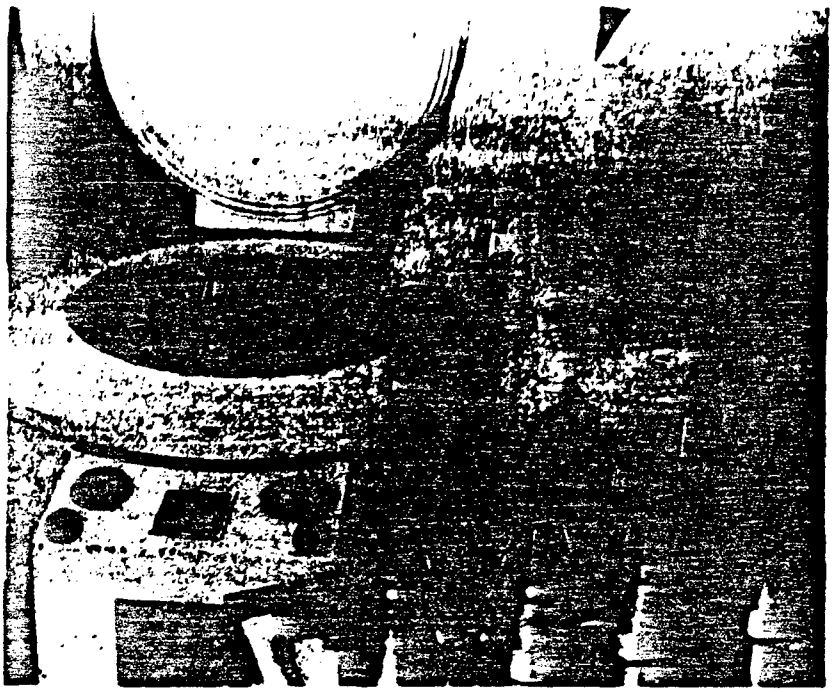
Although little attention was given in most laboratories to the hazards connected with the centrifuging of infectious cultures, a few laboratories had taken steps to control or lessen these hazards. The measures taken are described below.

In several laboratories it was indicated that acid digestion of tuberculosis sputum had been stopped because spilled acid gradually corroded away the bottoms of the centrifuge cups. Other laboratory directors emphasized the necessity for frequent inspection of the centrifuge equipment. In 12 laboratories some type of safety centrifuge cup with tight fitting dome top was used. Figure 44, A shows the safety centrifuge cups used in one Swedish laboratory. These were manufactured in Germany by the Stock Company. They differ from the American-made item in that there is no rubber gasket to seal the dome to the body of the cup; a grease seal is used. Figure 44, B shows a smaller safety centrifuge cup used by an Australian scientist.

Six Scandinavian laboratories used table model centrifuges enclosed in ventilated compartments with sliding doors, as shown in Figure 45. Air is continually exhausted from each unit and an ultraviolet lamp lights when the door is closed. All centrifuge controls are located on the outside door. When the centrifuge is turned off, a switch prevents the compartment door from opening for five minutes, allowing time for the exhaust ventilation and the ultraviolet to remove infectious aerosol.

In several laboratories nonventilated cabinets were used to enclose centrifuge operations. These are illustrated in Figure 46. In three instances nonventilated compartments were used to enclose Sharples centrifuges, but the more frequent procedure was to provide a small isolation room for high speed centrifuges.

Some of the oldest laboratory centrifuges did not have a bowl and consisted of a motor and attached rotor hung by three chains from a stand made of metal rods. Such centrifuges not only offer no biological protection but present a serious mechanical hazard. In five European laboratories chain-hung centrifuges were still in operation.



A

B

Figure 44. Safety Centrifuge Cups.
A. Cups Used in a Swedish Laboratory.
B. Cups Used in an Australian Laboratory.

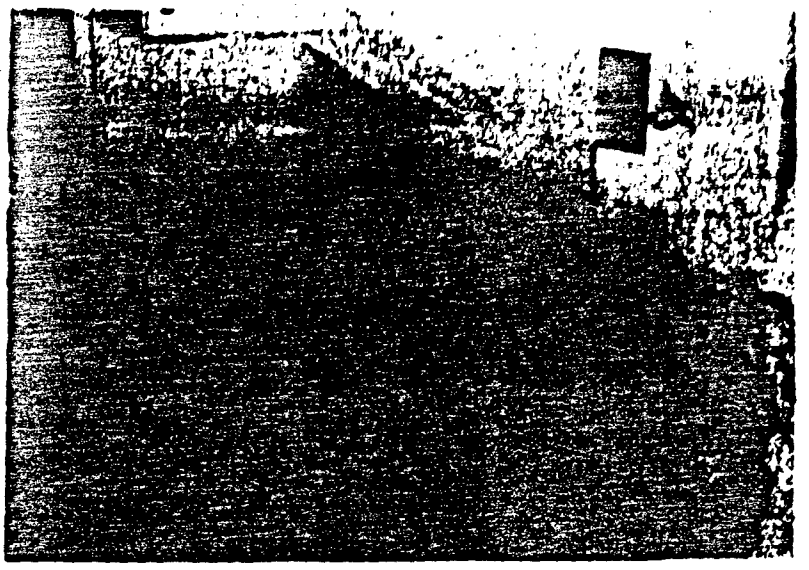
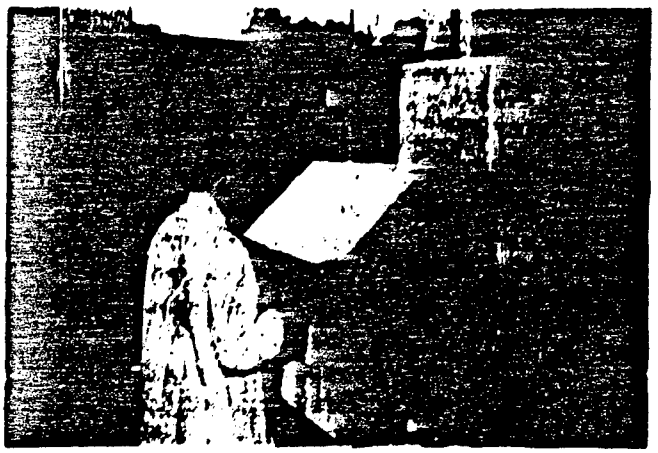


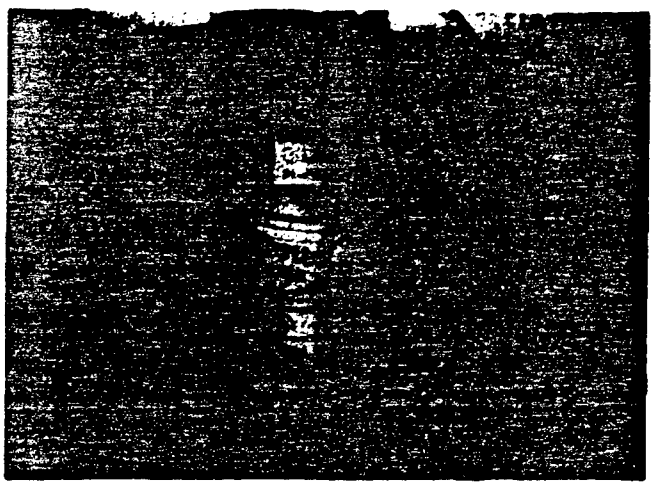
Figure 45. Ventilated Centrifuge Compartments.

It is significant that many laboratory directors felt that the use of centrifuges which did not require balancing of the cups reduced the hazard of breakage. Non-balancing type centrifuges were used in 19 European laboratories. At least one scientist felt that centrifuges in which the cup is held to the turning head by a universal type joint decreases the hazard of breaking centrifuge tubes. According to this theory the principal breakage hazard occurs when the centrifuge is gaining speed or slowing down.

Realizing the hazards of centrifuging tuberculosis sputum samples, several scientists had devised alternate means of protecting themselves. For example, centrifuge tubes sometimes were encased in blocks of rubber or other material or in a covered metal can before centrifuging. In one laboratory not only were the sputum tubes encased in a rubber block before centrifuging, but each individual screw cap was sealed with a plastic material and tested for leakage with an indicator sensitive to the sodium hydroxide digesting solution.

At the Imperial Chemicals Industries Laboratories, centrifuges for infectious work were located in large ventilated hoods equipped with a filtered exhaust and ultraviolet lamps.





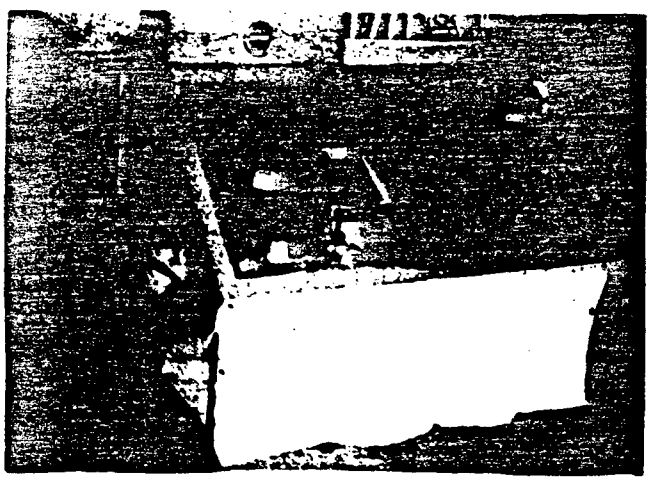


Figure 46. Nonventilated Centrifuge Enclosures.

C. GAS STERILIZATION TECHNIQUES AND APPARATUS

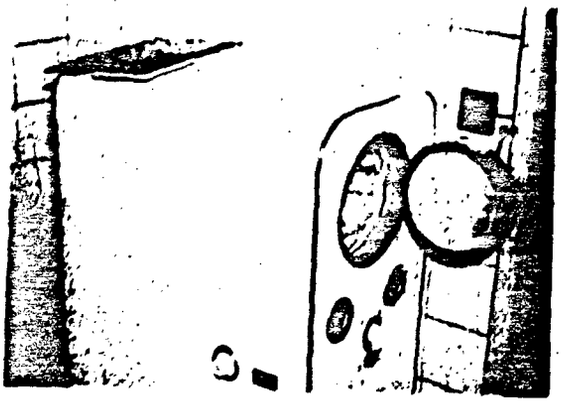
1. Ethylene Oxide

Commercially available chambers for sterilizing materials with mixtures of ethylene oxide gas were seen in two laboratories; the Statens Seruminstitut in Copenhagen and Aurora Hospital in Helsinki. I subsequently visited the manufacturer of each instrument. Studies on ethylene oxide sterilization methods were being carried out in laboratories in England, Scotland, Germany, Denmark, Italy, The Netherlands, Norway, and Switzerland.

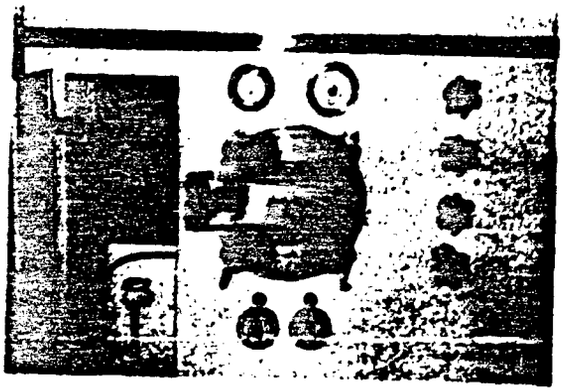
Scientists at the Statens Seruminstitut in Copenhagen were testing the German-made sterilizer shown in Figure 47, A. This apparatus is manufactured in Mainz, Germany by Med. ABT and is called the DMB-Sterivit. Original tests with the sterilizer were done at Johannes Gutenberg-Universitat in Mainz.[42] Chambers are available in various sizes. The one pictured cost 6000 Danish kroner (about $1000.00). The chamber is filled to a pressure of five atmospheres (about 75 psig) from a small pressure cylinder (about 25 lbs) containing a mixture of 13 per cent ethylene oxide and 87 per cent carbon dioxide. There is no prior evacuation. Chamber temperatures can be regulated between 35° and 65°C. Exposure times as short as 15 minutes are supposed to be sufficient for sterilization. At the end of the exposure period the machine exhausts the chamber gases through an absorbing calcium chloride solution. Using heavy suspensions of bacterial spores dried on sand, the preliminary tests at Statens Seruminstitut required an exposure period of at least four hours for complete inactivation.

Working with the Finnish manufacturer, OY, Santasalo - Sohlberg AB, Dr. Odd Wager at the Aurora Hospital in Helsinki was investigating the use of ethylene oxide - Freon mixtures for the sterilization of blood transfusion sets. The apparatus manufactured by Santasalo - Sohlberg is shown in Figure 47, B. The cylindrical shaped chamber has a volume of about 50 liters. Smaller (25 liters and 15 liters) and larger vessels are also advertized. A mixture of ten per cent ethylene oxide in Freon, Freoxid, packaged in disposable cans is used to charge the sterilizing chamber. This mixture is almost identical to several products made in the U.S. The container is shown in Figure 47, C.

Before admitting the sterilant, the chamber is evacuated to 29 inches of mercury. An electrical heating apparatus raises the chamber temperature to 55°C, and the gas mixture along with some moisture from a spray device is admitted to the chamber. With a maximum ethylene oxide concentration of 1200 milligrams per liter, sterilization should be complete in one to two hours. A final pressure of about 25 psig is developed in the chamber. The manufacturer suggests the use of Royce's sachet indicators to check sterilization. Dr. Wager stated that on the basis of the tests conducted the Red Cross had proposed that ethylene oxide be used to sterilize all blood transfusion sets used in Finland.



A



B

C

Figure 47. Ethylene Oxide Sterilization Apparatus.
A. Sterivit Apparatus.
B. Santasalo Apparatus.
C. Santasalo Freoxid Can.

In England the Medical Research Council had organized a working committee to evaluate ethylene oxide sterilization methods. At the Central Public Health Laboratories in Colindale basic studies with pure ethylene oxide were being done in glass desiccators. Test cultures with and without serum added were being dried onto cotton threads for exposure to quantitative amounts of the gas. Some of the studies, which are being directed by Dr. R. O. E. Williams, concerned the amount of moisture necessary for sterilization to occur. Dr. Williams was also cooperating with a local firm in the use of a German-made apparatus called the Degesch. This apparatus was made to rid materials of insects and is charged with a mixture of 90 per cent ethylene oxide and 10 per cent carbon dioxide. The machine was being used in tests to determine the best method of sterilizing hospital blankets. In this case, also, the scientists were concerned with the effect of relative humidity.

A closed metal cabinet used in England by Royce and Sykes for an aseptic area in which to do sterility testing[43] is sterilized with ethylene oxide. A quantity of liquid ethylene oxide sufficient to yield a gaseous concentration of 12.5 per cent (V/v) is poured on the floor of the cabinet and allowed to react for 16 to 24 hours. Being concerned with the hazard of skin burns by the ethylene oxide-treated gloves, Royce and Moore[44] conducted a study in which they found that the danger of burns could be obviated by flushing the gloves with air and allowing them to hang from the cabinet in free air for a minimum of one hour.

The question asked most frequently by British scientists was: What controls can be set up to insure that treated materials are sterile? At least a partial answer is provided by an indicator control packet for ethylene oxide sterilization developed in that country by Royce and Bowler.[45] The indicator packets are marketed by Boots Pure Drug Co., Ltd., Nottingham, England, and called "Royce's Sachets." They are made by sealing a quantity of a solution that will absorb and react quantitatively with ethylene gas within a small plastic bag. The plastic itself must absorb or pass quantities of gas sufficient to cause the desired reaction.

Five milliliter quantities of a saturated and acidified aqueous solution of magnesium chloride containing 0.004 per cent bromophenol blue are sealed into two-inch lengths of flat polyethylene tubing that is one inch wide and 0.005 inch thick. Reaction of ethylene oxide with the magnesium chloride forms ethylene chlorohydrin. The reaction is quantitative; that is a reaction sufficient to cause a color change will occur after the absorption of a certain quantity of gas. Since the gas is assumed to permeate the plastic film at a constant rate, the color change can be calibrated to represent the product of exposure time and concentration (the CT value referred to in publications in this field). Thus, for the sachet described above, the acidity, the indicator, the type of plastic and its thickness are such that a total CT exposure of 3800-milligram hours per liter of chamber space at 20°C should result in a color change of blue to yellow. Sachets for other CT values can be made by varying one or more of the components. The sachets are placed in a representative location in the exposure chamber and observed at the end of the treatment. Carbon dioxide or Freon, common diluents for ethylene oxide, do not affect the reaction.

The sachet principle can be used to make indicator devices for other gases. Royce and Bowler[45] reported that they have prepared sachets for detection of formaldehyde. Heseltine and Royce[46] have described a sachet for use with methyl bromide.

In Berlin, Germany, the Robert Koch Institute had been experimenting with Carboxide for about two years. They have been concerned principally with the procedures required to sterilize catgut and other hospital and surgical materials. In one series of tests with catgut samples exposed in a chamber at an ethylene oxide concentration of 1460 milligrams per liter and a relative humidity of 40 per cent, the samples were sterile in 15 minutes. At ten per cent relative humidity the samples were still contaminated after a one-hour exposure. The exposure temperature was 40° to 50°C. Catgut packed in polyethylene bags is normally treated for about four hours in a chamber which is not evacuated before admitting the gas. This institute also hoped to use ethylene oxide to sterilize books handled by tuberculosis patients.

The Sterility Control Laboratory of the Instituto Superiore di Sanita' in Rome tested packages of surgical catgut treated with ethylene oxide by commercial firms in that country. I was told that catgut samples reaching this laboratory which were treated with ethylene oxide were more consistently sterile than samples treated by other methods. In addition, quantitative tests had shown that the number of contaminants usually were fewer from a non-sterile, ethylene-oxide-treated sample than from non-sterile, heat-treated samples.

In Norway, the State Institute for Public Health has been assigned the job of evaluating ethylene oxide for use in sterilizing blood transfusion sets and other hospital items.

In Switzerland, the Swiss Serum and Vaccine Institute was investigating the possibility of using ethylene oxide to sterilize large lyophilizing machines which are used to dry vaccines and antisera.

2. Formaldehyde

Formaldehyde was the most frequently used gaseous disinfectant in the laboratories visited during the fellowship. Those who used formaldehyde to decontaminate equipment and rooms seemed to be well acquainted with the proper methods of application. Two recent British publications on formaldehyde disinfection [47,48] are read and accepted as the standard in many European laboratories. These publications, one of which was prepared by Dr. H. M. Darlow at the Microbiological Research Establishment (MRE) in Porton, England, describe the use of formaldehyde for various disinfection procedures.

A simple device designed at the MRE laboratories for vaporizing small quantities of formalin in a closed cabinet is shown in Figure 48. The vaporizing chamber is a two-inch diameter metal pipe attached to the

cabinet or chamber to be decontaminated. A small metal funnel and a valve is provided for the introduction of formaldehyde solution to the closed pipe elbow. A burner is placed under the pipe to vaporize the solution.

A larger device called the formaldehyde boiling pot developed at the same laboratory is shown in Figure 49, A. This apparatus is used to generate formaldehyde fumes for the decontamination of rooms and other large spaces. It is about nine inches in diameter, ten inches high, and is made of stainless steel. The electric heater in the bottom is operated through a timing switch. As a safety device, a kick-out plug is also provided.

Small electric vaporizers as shown in Figure 49, B were used in cabinets or rooms in several European laboratories for producing formaldehyde vapors. The apparatus shown is the Aerovap made by Shepherds Aerosols, Ltd., Tunbridge Wells, Kent, England.

Figure 50 is a sketch of a formaldehyde fumigation box developed at the MRE laboratories. It is used for the decontamination of laboratory equipment and aerosol masks. The box is mounted on wheels for portability. At the end of a 2.5-hour exposure period the exhaust tube must be run to the outside so that the chamber can be air-washed to free it of noxious fumes.

3. Propylene Oxide

Since quantities of ethylene oxide greater than a few milliliters could not be obtained in Australia, scientists in that country were developing propylene oxide as a gaseous sterilant. This compound boils at 35°C, as compared with 11°C for ethylene oxide, and its sterilizing power is considerably lower than that of ethylene oxide. A. E. Atherton and Sons Pty, Ltd., Melbourne, were developing gas mixtures of propylene oxide to be used in appropriate exposure vessels. Mixtures being considered were (a) 11 per cent propylene oxide and 89 per cent Freon 11 and 12, and (b) 10 per cent propylene oxide and 90 per cent carbon dioxide. Several Australian laboratories were using propylene oxide for the cold sterilization of books and other materials. The usual procedure was to put a quantity of liquid propylene oxide in a beaker in a suitable vacuum chamber along with the material to be treated. The vessel is then evacuated and held overnight.

H. INOCULATING LOOP SAFETY

Microbiologists use the inoculating loop for a variety of manipulations involving the transfer of cultures and the inoculation of media. Lengths of platinum or nichrome wire are inserted into a suitable holder and a small loop, usually 3 to 4 millimeters in diameter, is formed at the distal end of the wire. Phillips and Reitman[49] have summarized the infectious hazards involved in using the inoculating loop. Using tracer microorganisms, almost

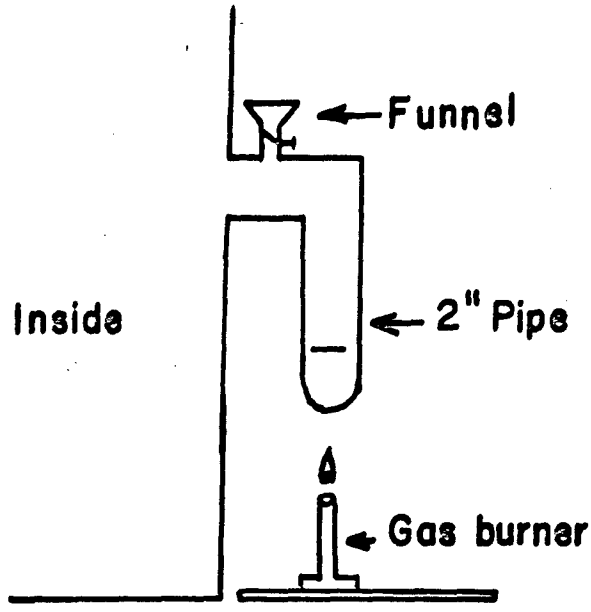
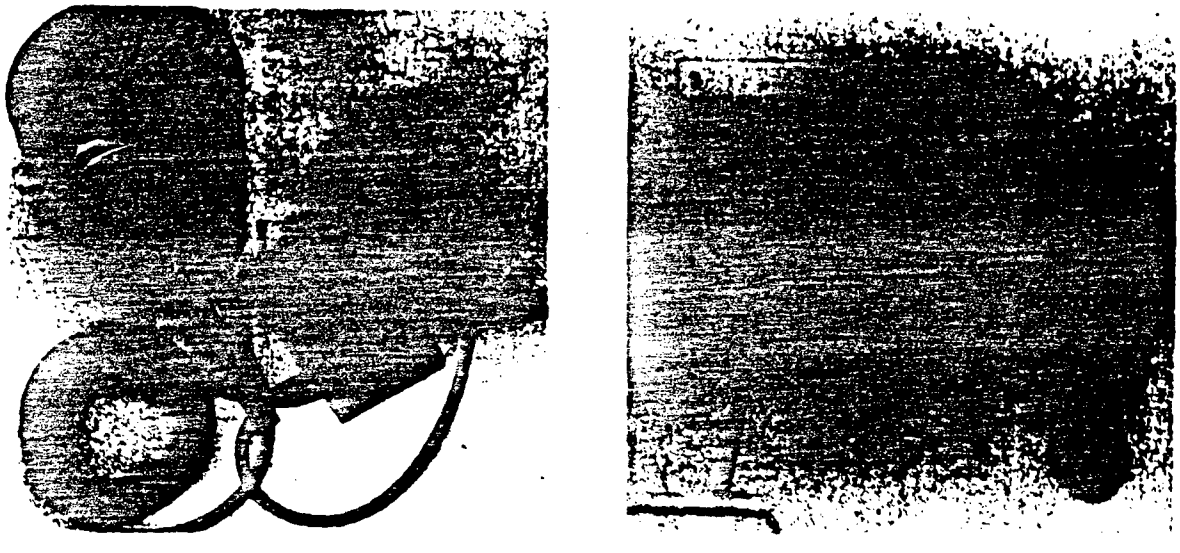


Figure 48. Cabinet Attachment for Vaporizing Formalin.



A B

Figure 49. Formalin Vaporizing Apparatus.
A. Formaldehyde Boiling Pot.
B. Wall Vaporizer.

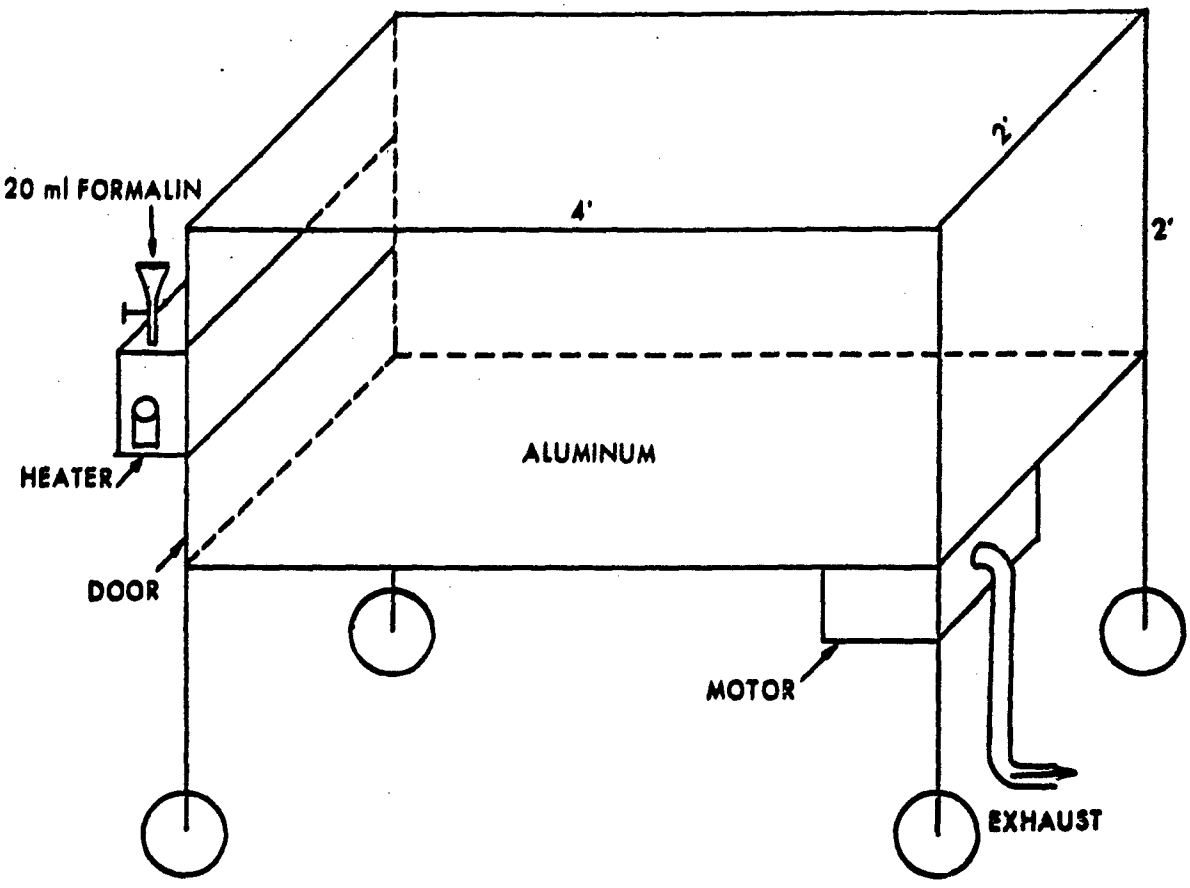


Figure 50. Formaldehyde Fumigation Box.

all common techniques tried resulted in the release of some aerosolized bacteria. The techniques tested included (a) flaming a loop after use, (b) inserting an inoculating loop into a broth culture, (c) bursting a film in an inoculating loop, (d) streaking agar plates with inoculating loops, and (e) shaking a loopful of culture in a test tube.

A recent British publication on precautions for the tuberculosis laboratories[40] lists three methods of controlling the hazards presented by flaming inoculating loops:

1. Treatment of the loop in boiling water, in a strong disinfectant, or in hot oil at 150°C before flaming.

2. Use of shields or hoods on gas burners (loop incinerators).

3. Substitution of disposable applicators or cotton swabs for transferring cultures, making slides, etc.

This publication states that of the many loop incinerators that have been developed, some have not been tested experimentally and others "are known to have proved unsatisfactory." Some type of loop incinerator

device was seen in 21 laboratories. Some were of commercial manufacture, but most were of original design. Figure 51 shows examples of these loop incineration devices. Those shown in Figure 51, A, B, and C have been tested and found to be satisfactory.

Figure 51, A is the loop incinerator developed at the U.S. Army Biological Laboratories. This device is commercially available and is used in a number of U.S. laboratories. B shows a device designed and tested by Darlow[50] in England. C is a loop incineration chamber developed by Dr. Hans Engbaek at the Statens Seruminstitut in Copenhagen. This device was seen in three European laboratories. Examples of some homemade loop flaming devices used in European laboratories are shown in D, E, and F. In most instances these were made by laboratory technicians who observed the splattering of culture material when flaming inoculating loops.

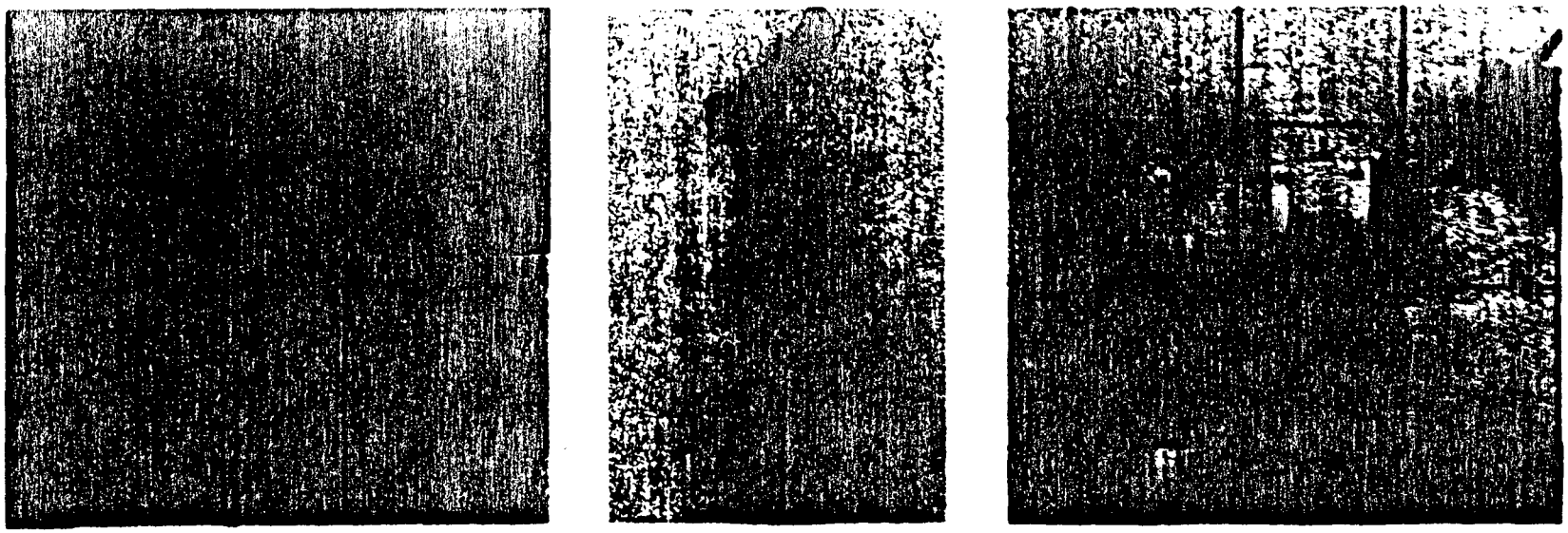
In several laboratories it was customary to provide a beaker filled with sand and alcohol to clean inoculating loops. By stabbing the sand-alcohol mixture with the loop, most culture material is scraped off before the loop is sterilized in the flame. In one tuberculosis laboratory a small electric heater kept a flask of water boiling. After using a loop, technicians were required to hold it in the boiling water for five seconds before resterilizing in the gas flame.

In one U.S. laboratory sterile, wooden swab sticks were used in place of inoculating loops to make culture transfers. After use the sticks were discarded into a disinfectant solution. At the Municipal Bacteriological Laboratory in Gothenburg, Sweden, stainless steel transfer loops were wrapped in paper and sterilized by heat. Each loop was used once and placed in a disinfectant solution. Used loops were then autoclaved, cleaned, and resterilized for use.

Kovacs[51] has described the use of spiral wire loops in connection with a micro-method for detecting indol. The spiral loop is shown in Figure 52. Using 22-gauge platinum wire the spiral is made by shaping coils around a metal screw of appropriate diameter (approx. 5/32 inch). A short length of straight wire is left at the beginning which can be doubled back through the center of the coil. The spirals are pressed closely together so as to hold fluid more easily. Transfer loops of this type were used in several laboratories. They generally hold about 0.1 milliliter or more of fluid. Although they eliminate the use of pipettes for the transfer of small amounts of fluid, because of the ease of splattering or splashing, they should not be used with infectious microorganisms except in a ventilated cabinet.

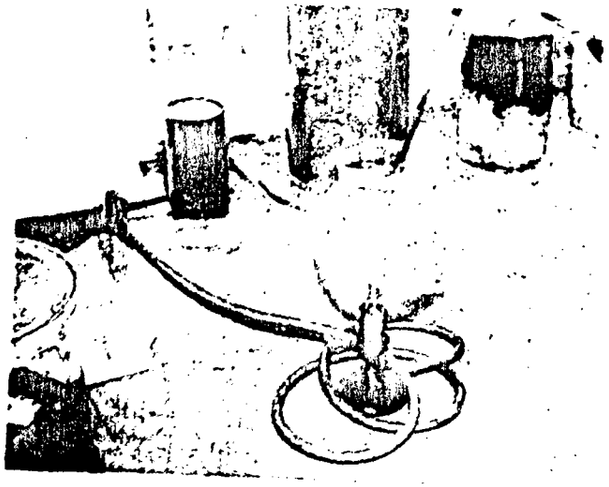
I. LYOPHILIZATION

In 1954 Reitman, et al.,[52,53] at the U.S. Army Biological Laboratories, described the potential hazards involved in the lyophilization of infectious cultures. It was shown that the lyophilizing apparatus becomes heavily contaminated during use and that the hands of the operators usually become

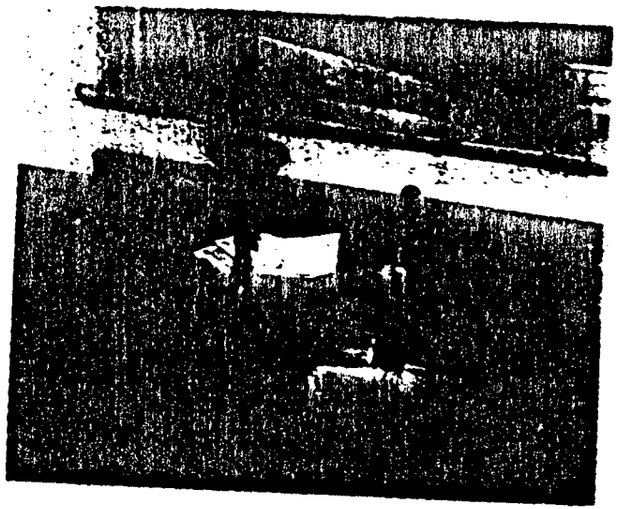


A B C

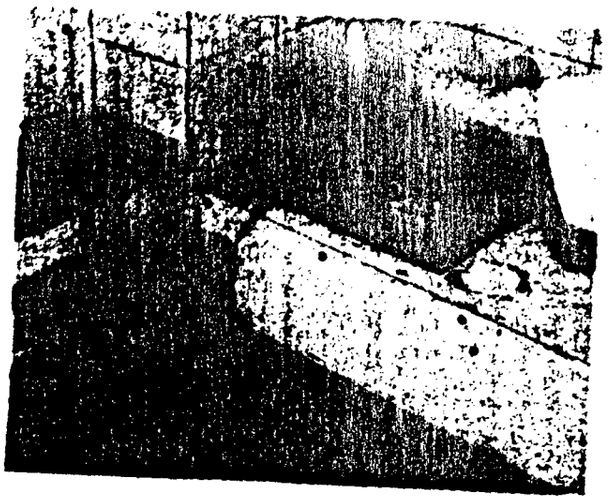
Figure 51. Loop Incinerators.
A. U.S. Model.
B. Darlow Loop Incinerator.
C. Englbaek Loop Incinerator.



D



E



F

D, E, and F. Homemade Loop Incinerators.

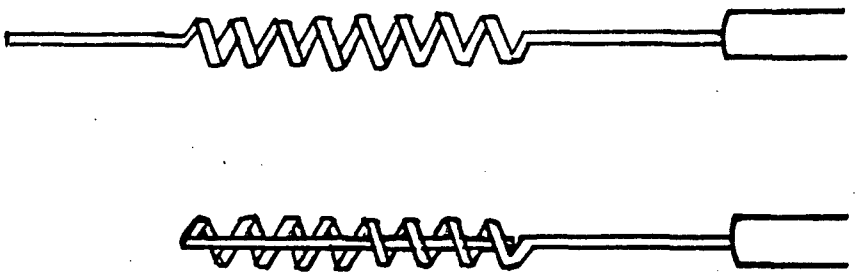


Figure 52. Spiral Loop Device.

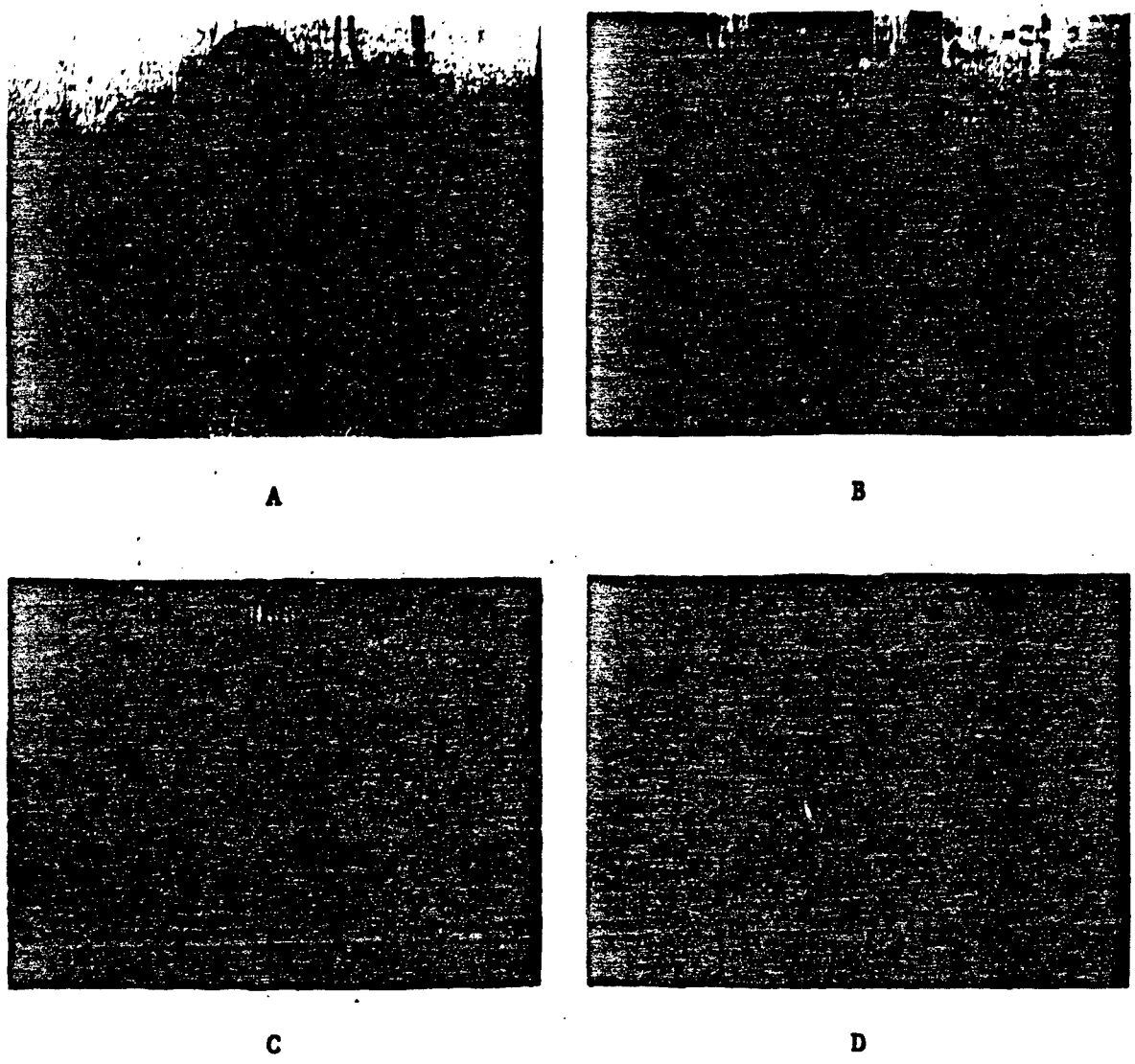
contaminated when removing ampoules. Although test organisms were not recovered from the oil in the vacuum pump of the apparatus, it was demonstrated that organisms do reach this area. A cotton filter was therefore devised which prevented contamination of the pump, assured that no contamination escaped from the pump exhaust, and provided a convenient place to disconnect the contaminated portion of the lyophilizer for sterilization.

Lyophilization procedures were carried out in 43 of the 102 laboratories. Only in five instances were the apparatus and procedures adequate in light of the recommendations advanced by Reitman, et al. In 14 European laboratories, centrifuge lyophilizing apparatus of the type shown in Figure 53, A were used. Several firms used larger commercial models as shown in B. In the design of these instruments little consideration had been given to means of sterilizing the manifolds or preventing contamination of the exhaust pump system. Simpler laboratory lyophilizers of the type more often used are shown in pictures C and D. Laboratory personnel often sterilized the manifold portion of this type of apparatus, but only rarely was a filter used to protect the pump system. In several laboratories the pump exhaust air was discharged to the outside of the building. Two laboratory directors felt that during operation the pump oil would reach a sterilizing temperature.

In most laboratories in which observations were made, considerable care was exercised in opening vials of lyophilized infectious microorganisms. When a cabinet was available it was almost always used. In several virus laboratories, however, vials were opened with no regard for the mechanical or infectious hazards which might be created.

J. MICROSCOPE SAFETY

Realizing that bacterial cultures prepared on slides and stained for microscopic examination may contain viable organisms, several laboratory directors insisted that microscope objective lenses be wiped periodically with a liquid disinfectant. One British laboratory was prepared to decontaminate microscopes with vapors of formaldehyde. In Australia, one



A B C D

Figure 53. Lyophilizing Apparatus.
A. Centrifuge-Lyophilizing Apparatus.
B. Commerical Lyophilizer.
C and D. Laboratory Lyophilizers.

director objected to the use of microscope immersion oil bottles of the type that require a glass rod to be touched to the microscope slide. He felt that the oil, which is probably a good preservative, might become contaminated with viable organisms from the slide. To avoid this he used an immersion oil dispenser made by Elliott's Liverpool, Ltd., Liverpool, England, which precludes touching the slide with the dispenser bottle.

More serious hazards, however, occur in the preparation and staining of slides for examination. Particularly in routine laboratories where large numbers of slides are prepared (e.g.: for detection of tubercle bacilli), this may spread contamination. The following points of possible hazard were noted in one or more infectious disease laboratories.

1. The initial transfer of culture material to a glass slide is often a probable source of environmental contamination. Sometimes too much fluid is placed on the slide and an excess runs off, contaminating the table top or sink and the hands of the technician who subsequently handles the slide. Only occasionally were technicians observed to be wearing rubber gloves. The practice of mashing two slides together to crush sputum material is a particularly flagrant disregard of good laboratory practice when done on the open table top. Dekking,[54] at the University of Amsterdam, investigated the hazards arising from this technique. Photographically he was able to demonstrate the formation of aerosol particles when the slides were crushed together and recommended that the technique not be used.

2. How slides are handled after the smears are made and before they are heated or fixed is important. One wonders how much air-borne contamination can result when slides are left to air dry on the bench; perhaps overnight. Certainly the use of an electric fan, as observed in one instance, should not be tolerated.

3. Because of the varied resistance of microorganisms to heat and chemicals and because of the many fixing and staining techniques employed, it is not valid to assume that stained preparations are always free of infectious forms. Haphazardous handling of stained preparations of infectious microorganisms was frequently noted. Furthermore, slides were not always sterilized before discarding.

4. The staining sink is another potential source of infection because viable organisms can be washed off of the slides with the fluids used. A commonly recommended technique is to stopper the staining sink and fill it partly with liquid disinfectant solution. All too frequently slides were stained over an empty and unplugged sink.

For the most part, even when ventilated cabinets were available, the preparation and microscopic examination of slides took place on the laboratory bench. In several tuberculosis laboratories the smears were made and dried in a cabinet and then stained and examined on the bench. Some systematic critical evaluation of the safety of these techniques seems desirable.

K. PIPETTE AND SYRINGE SAFETY

Pipettes and syringes are among the most frequently used laboratory devices. In 1955 Reitman and Phillips[55] summarized experiments done at the U.S. Army Biological Laboratories which demonstrated pipetting hazards and recommended the following safety rules:

"1. If possible, enclose pipetting operations in a ventilated safety cabinet or hood.
2. Avoid oral pipetting of dangerous materials — use a pipettor.
3. Do not blow out the last drop from pipettes.
4. Do not mix dilutions by blowing air through the pipette into the culture.
5. Place a disinfectant soaked towel on the working surface and autoclave the towel after use.
6. Use flat pans containing disinfectant for the discard of pipettes. Autoclave pan and pipettes together after use."

In the same manner Hanel and Alg[56] summarized the studies of Wedum[57] and others on the hazards connected with the use of the syringe and needle in bacteriological and virological procedures. They recommended the safety rules listed below:

"1. If possible, when working with infectious microorganisms, use the syringe and needle only in a ventilated safety cabinet or hood.
2. Use only Luer-Lok type syringes.
3. Wear surgical or other type rubber gloves when using the syringe and needle.
4. When removing aliquots through vaccine bottle stoppers, wrap the stopper and needle in a cotton pledget soaked in 70 per cent alcohol or in a proper disinfectant.
5. Expel excess liquid and bubbles into a large cotton pledget soaked in a proper disinfectant.
6. Discard syringes into a pan of disinfectant without removing the needle or squirting out the residual culture.
7. Before and after injection of an animal, swab the site of injection with a disinfectant."

In 62 per cent of the laboratories visited workers were allowed to mouth-pipette infectious or toxic suspensions; 38 per cent of the institutes had a rule prohibiting oral pipetting. Some laboratory directors took the position that the individual scientists or workers could decide if and when oral pipetting was to be avoided and that establishing a general rule was not in keeping with good management practice. Some laboratory workers did avoid mouth pipetting although not required to do so. Some had had pipetting accidents or had known others who had become infected in this manner. However, some workers indicated that since others in their laboratory did not use pipettors to avoid mouth pipetting, they felt reluctant to do so. (In effect, they might be laughed at.) Two other objections were voiced: (a) available pipetting devices are awkward and difficult to use, and (b) using pipettors slows up the work.

Among those laboratories where pipetting devices were used, rubber bulbs most frequently served as the pipettor. In several laboratories rubber tubing was used as shown in Figure 54, A. B and C show devices being used in two German laboratories. The pipettor in B, which is used in virus manipulations, uses an all-metal bellows which is operated by a screw handle. D shows pipettors used in a Swedish virus laboratory. Other devices used in small numbers of laboratories were:

1. Propettes. This type of pipettor is sold in Europe under several names: England: The Griffin Pipette Filler, Griffin and George (Sales), Ltd., London. Germany: The "Peleus-Ball," Walter F. C. Ebel, Molln, Llg. 2.

2. "Pi-Ka" pipettors, Walter F. C. Ebel Company.

3. "Fortuna" pipettors, Walter F. C. Ebel Company. This type of pipettor is similar to a closed syringe which is attached to the upper end of the pipette (Figure 55).

Although serological or volumetric type pipettes were used in most laboratories, in Australia and in many of the European laboratories Pasteur pipettes were also used. Pasteur pipettes are made by drawing out short lengths of glass tubing so that a long narrow tip is provided. The pipettes are not placed in the mouth but are normally operated by small rubber bulbs, called teats, placed over the larger opening. Today this type of pipette is rarely used in American laboratories. Among 72 laboratories outside of the American Continent, 57 per cent used Pasteur pipettes in some phase of the laboratory operations.

Even though mouth pipetting is avoided with Pasteur pipettes, another potential and obvious hazard was observed. Undoubtedly with careful and expert use, splattering and foaming at the tip of the pipette can be avoided. Also a careful worker would not expell the last drop from the pipette with force. However, in routine diagnostic laboratories, it was obvious that the use of Pasteur pipettes frequently created definite hazards.

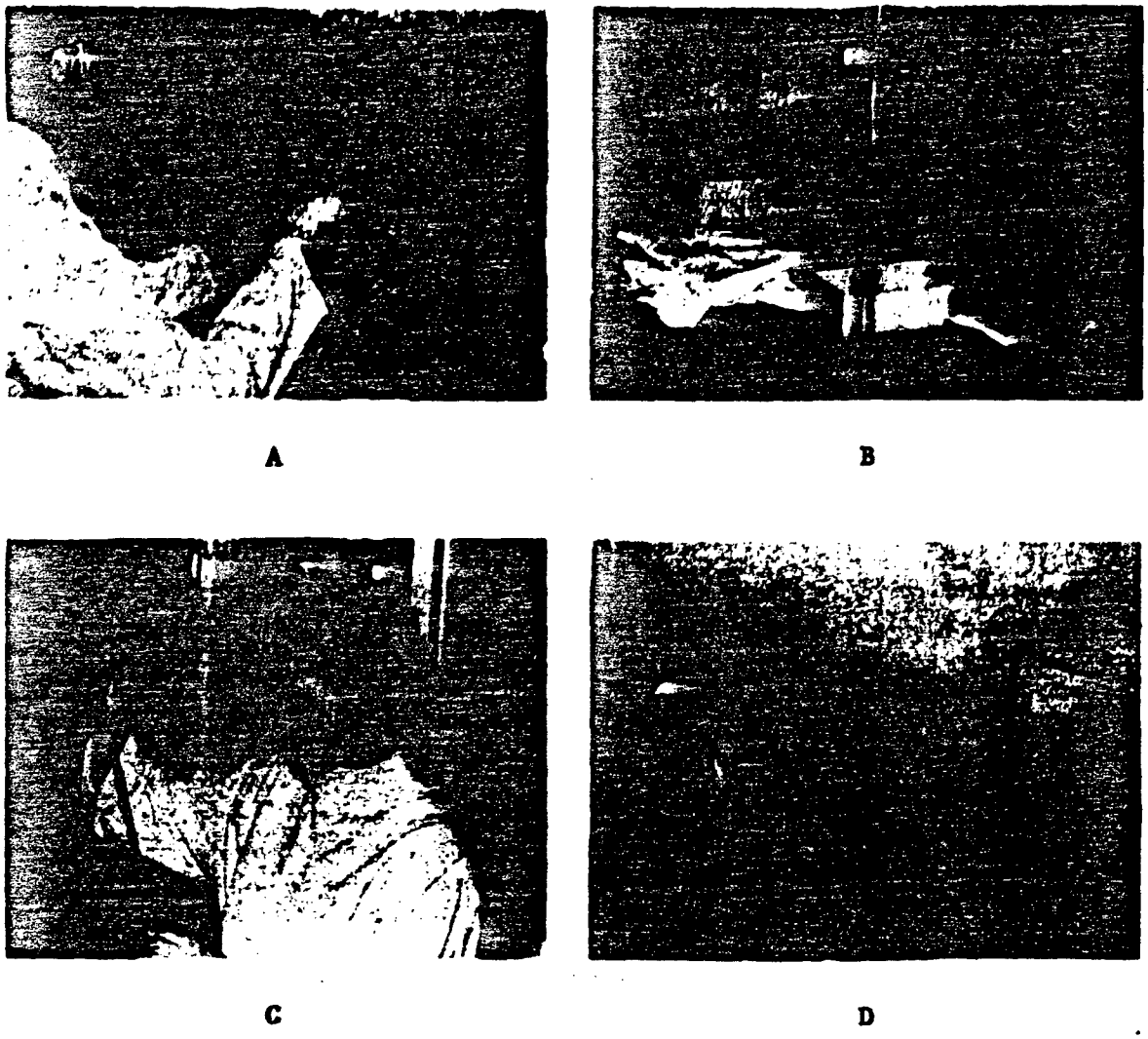


Figure 54. Pipettors.
A. Tube Pipetting.
B, C, and D. Mechanical Pipettors.

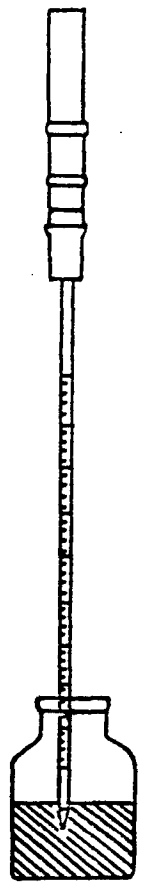


Figure 55. Syringe Pipettor Device.

For example, they frequently were used to wash growth of Mycobacterium tuberculosis from agar slants, preparatory to doing strain sensitivity tests. Technicians doing this work generally have a large number of tests to perform in one day. The bubbling and splashing from the hurried and too vigorous use of the bulb is most undesirable. Another obvious danger is the hazard of self inoculation from the sharp-tipped, capillary tubes. It is best not to use Pasteur pipettes with infectious disease agents.[23]

Observations were recorded on the methods for discarding contaminated pipettes and syringes. The classical method is to provide, on the laboratory bench, a glass museum jar filled with disinfectant solution. The jar has a layer of glass wool in the bottom to prevent breakage of the tips of the pipettes. Since the jars can not be autoclaved the pipettes must be fished out and placed in another container for sterilization. In some laboratories it is assumed that the disinfectant is completely effective and the pipettes are taken directly to the wash room. In a few tissue culture laboratories only distilled water was used in pipette discard jars. A further disadvantage of upright jars is that the pipettes are frequently

not completely emersed in the liquid. Also the top edges of the jars can become contaminated from sliding pipettes over the edge. Glass jars break easily and plastic jars, like the glass, are usually not autoclavable. The safest and most desirable technique uses flat, autoclavable pans containing a germicidal solution. In this manner pipettes, syringes, and other small contaminated items can be completely emersed in the germicide and in this position be autoclaved before removal. In 24 per cent of the laboratories (20 of 82) this method was used. In 76 per cent non-autoclavable, plastic or glass jars were used for pipette discard. In several laboratories the jars were placed on the floor at the side of the technician, a position where they were especially prone to be turned over or broken. Much to the embarrassment of one laboratory director this happened while I was inspecting his laboratory.

Figure 56 illustrates the various types of pipette and syringe discard containers used in the laboratories. Most were similar to those shown in Figure 56, A, B, C, and D. The stainless steel container in E is typical of those in the Scandinavian countries. Undoubtedly the increased use of ventilated safety cabinets has been responsible for changing the method of disposal of pipettes, since upright glass museum jars are difficult to move in and out of cabinets. However, a hazard observed in a number of laboratories was due to the fact that the ventilated cabinet provided was too small. When manipulations were being carried out no space was available for a pipette discard tray and it was placed outside the cabinet. Each time a pipette was used it was removed from the cabinet for discard. In two foreign laboratories the situation was slightly improved by locating the discard tray immediately below the front edge of the cabinet as shown in F.

Figure 57 shows a rubber pipette pot used in some British laboratories. The pipette pots are marketed by P. B. Cow and Co., Ltd., 12 Hay Hill, Berkeley Square, London. The autoclavable discard container was designed by scientists at the Microbiological Research Establishment in Porton, England.

When a pipette is inserted into a culture and removed, the outside of the pipette and its tip become contaminated. If the pipette is then put into another flask the opportunity exists to contaminate the edge or outside of the flask or any other object which may come in contact with the pipette. Also, not infrequently, drops of fluid from the tip fall and contaminate surfaces. When using pipettes in diagnostic operations there is frequently an opportunity to cause accidental cross-contamination of samples. Because of these observations and because he did not have a ventilated safety cabinet, the director of one tuberculosis laboratory devised a hood which was attached to his pipettes and used when transferring reagents and cultures. This is shown in Figure 58. A glass hood device large enough to fit over the end of the test tube or flask is attached to a rubber tube and the tube is attached with rubber bands to the pipette. In this manner a small "closed system" is created during the actual transfer of liquids.

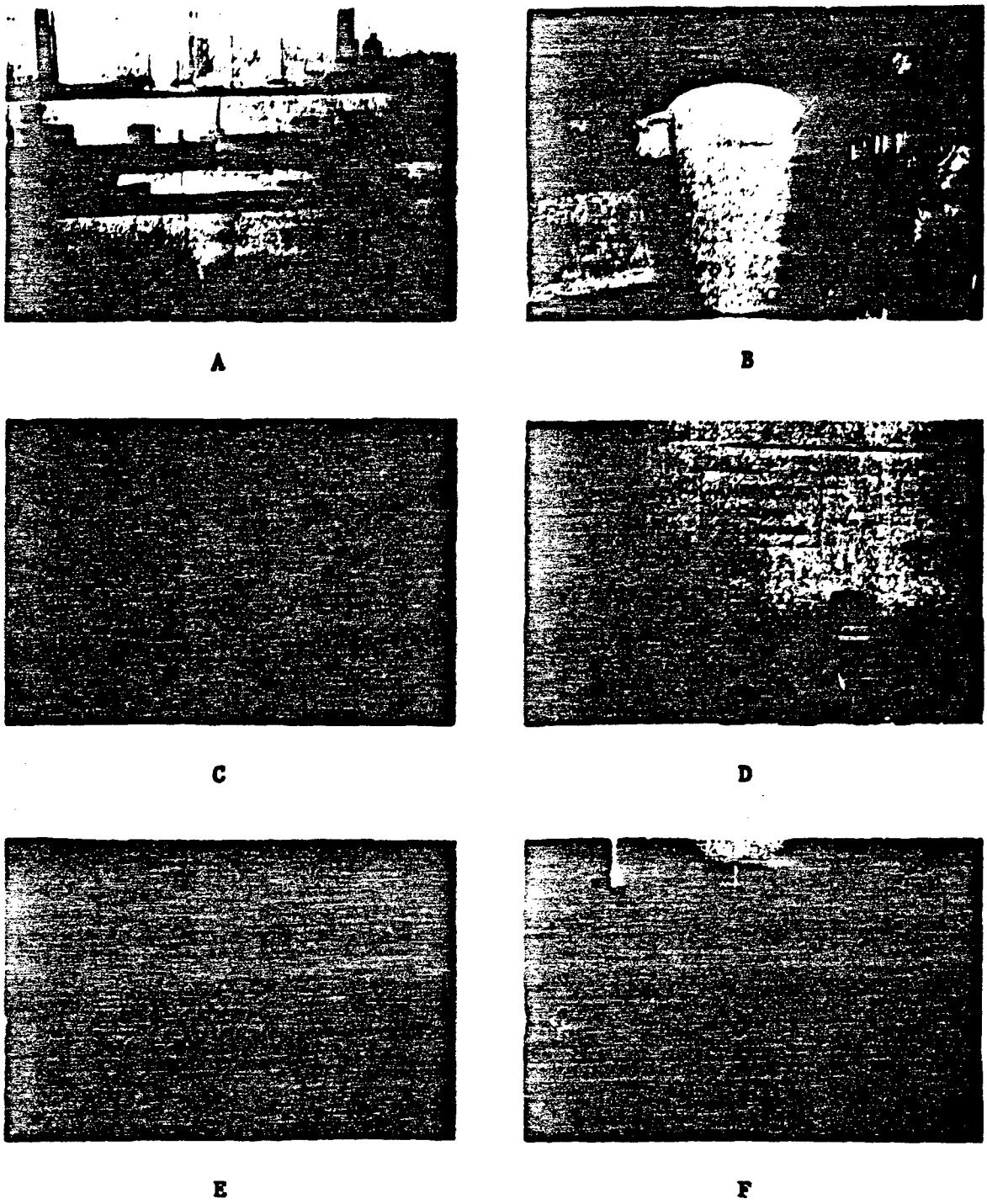


Figure 56. Pipette Discard Containers.
A. Glass Museum Jars.
B and C. Plastic Jars.
D. Jar for Pasteur Pipettes.
E and F. Metal Discard Pans.

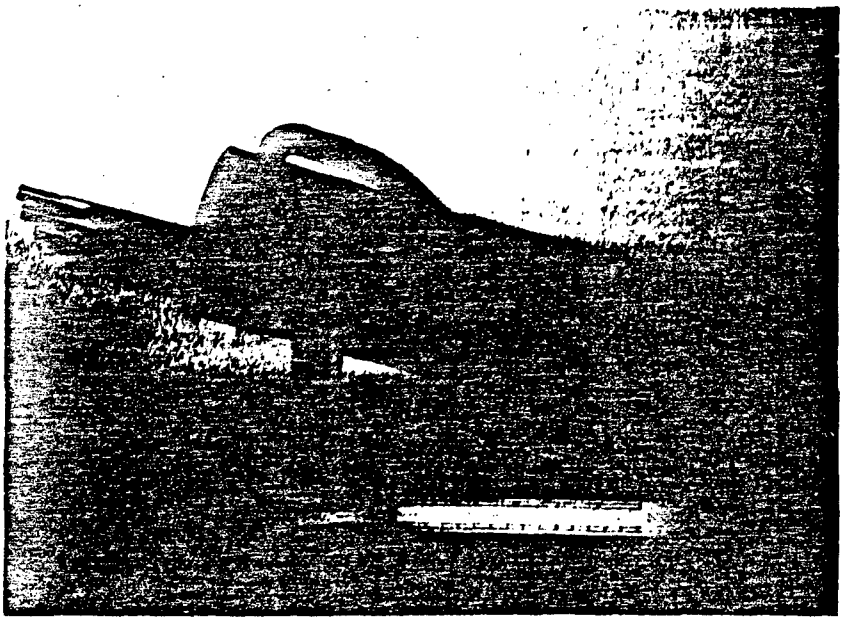


Figure 57. Rubber Pipette Pot.

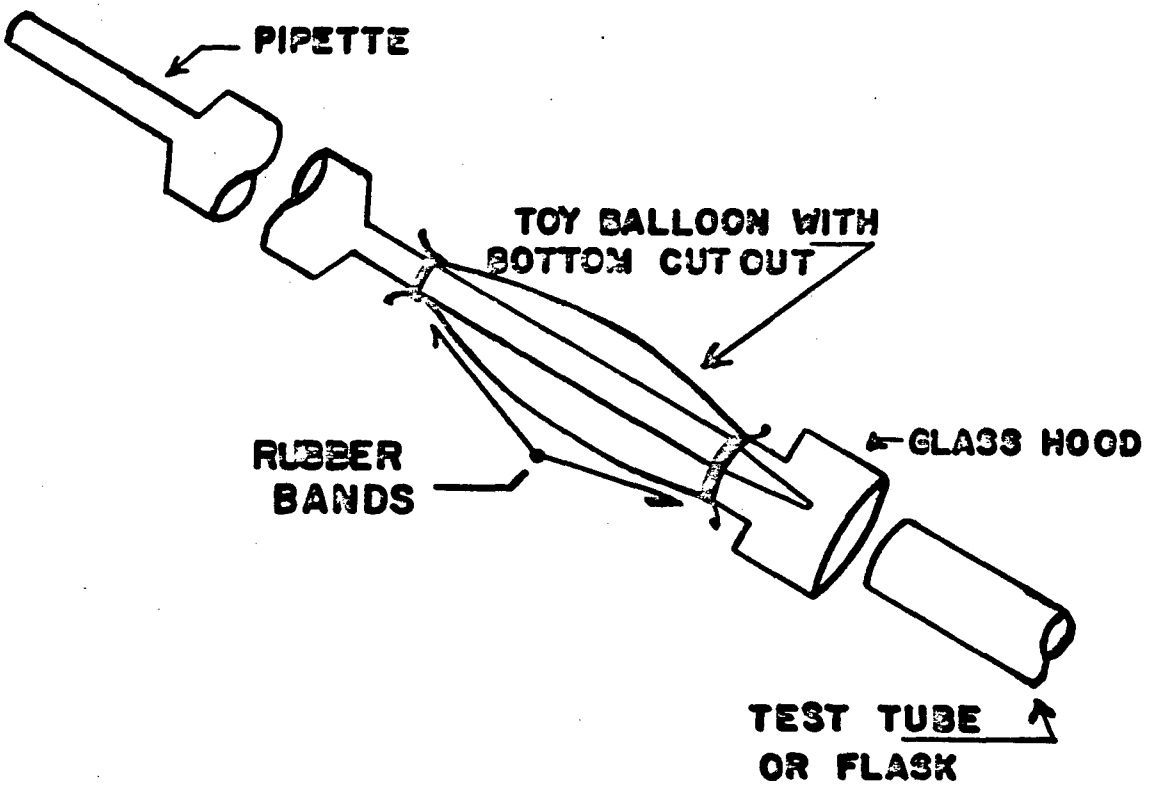


Figure 58. Pipette Hood Device.

At most laboratories I demonstrated the use of a simple but efficient pipetting device developed at the U.S. Army Biological Laboratories called the R. M. Pipettor.[58] Scientists and workers in a majority of the laboratories seemed pleased to learn of this device, and a number of requests for further information were received.

Unfortunately few laboratories used needle-locking type syringes exclusively, and many laboratory directors were not aware that tuberculin syringes with needle-locking devices are available. Needle-locking syringes were observed in only 30 of the 102 laboratories.

In one Australian laboratory the director was not satisfied with the common practice of expelling excess syringe fluid into a wad of cotton held between the fingers. He felt that this practice was dangerous because (a) the fingers of gloved hands may become contaminated, and (b) there is a likelihood of self-inoculation. The device shown in Figure 59 is said to eliminate these dangers. One-ounce, flat bottom, screw top bottles (British universal containers) are filled with absorbent cotton, the caps put on, and the bottles sterilized by autoclaving. Quantities of the bottles were prepared and used when injecting guinea pigs with sputum samples. Excess fluid and bubbles from a syringe are expelled into a bottle, the bottle is capped and subsequently resterilized. A scientist in one Canadian laboratory recommended that when using a syringe and needle the free hand or the hand used for holding the animal to be inoculated always should be kept back of the needle tip.[23]

At the Lister Institute in London syringes are pressure tested once each month by the method described by Guld and Rud.[59] The apparatus used is illustrated in Figure 60. To pass the test, a tuberculin syringe filled with water must not leak more than six graduations in six minutes. Scientists at the Lister Institute have experimented with syringe pressures, and have found that two atmospheres (about 30 pounds per square inch) of pressure are required to raise an intradermal bleb on the back of a guinea pig.

L. TRANSPORTATION

In 82 laboratories some type of medical or public health diagnostic work was carried out. This necessitated the transportation of potentially contaminated specimens to the laboratory. In hospital laboratories most specimens were brought directly from the wards, but many hospital laboratories and all public health laboratories also received specimens by mail. In 26 of 82 laboratories (32 per cent), management had difficulty with containers for transporting infectious specimens. The most frequent complaint was that the containers were often leaking upon arrival at the laboratory. Diagnostic slips or other papers in the containers were often suspected of being contaminated. Several directors were concerned that prepared empty containers leaving their laboratories might harbor infectious microorganisms.

Figure 59. Method of Expelling Excess Syringe Fluid.

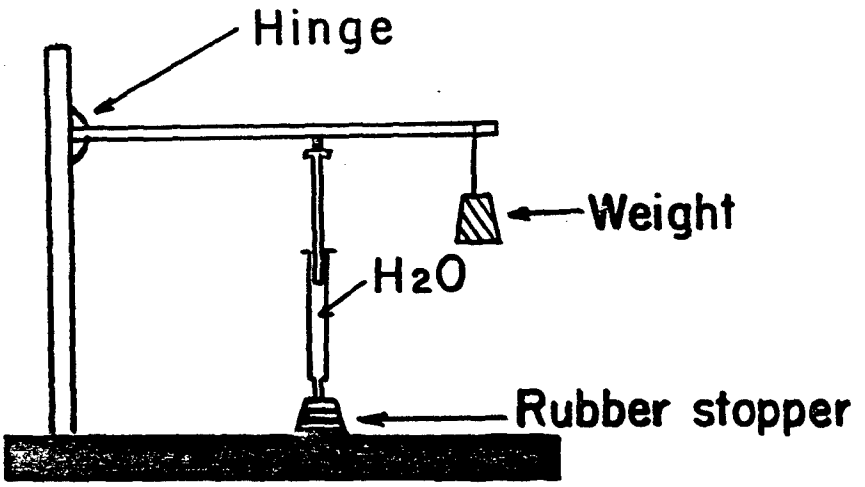


Figure 60. Syringe Testing Apparatus.

It is obvious that the hazards that may be created by poorly packaged cultures and specimens during and after transportation are being recognized by regulatory authorities. In the U.S., the Public Health Service and postal authorities have issued regulations governing shipments of infectious agents. In West Germany the Occupational Guild for Health Service and Welfare, which administers the compulsory accident insurance for all workers, issued, in 1956, an information bulletin on the transportation of infectious material. This bulletin is translated below in full:

"1. Every specimen (blood, urine, feces, sputum, pus, throat and nose swabs, biopsies, tissue, etc.) must be considered infectious, even if no suspicion exists initially.
2. Handle all of these substances very carefully and always wash your hands after touching them. Moreover, you endanger your fellow man if you do not pack, transport and dispatch these potentially dangerous specimens competently.
3. The dispatch or transport of the test material is permitted only in unobjectionable, unimpaired and corked (preferably with rubber stoppers) vessels. Such regulation containers are available from drug stores, hygienic institutes, medical research offices, and diagnostic laboratories. These containers must be filled without contaminating the outer walls with overflowing test material. If the outer wall should be contaminated, it must be disinfected.
4. During shipment, glass vessels must be packed so as to prevent breakage and, if possible, should be placed upright. Protection is offered by metal sleeves which, in their turn, are placed in wooden containers.
5. Be careful, also, during the unpacking of test material. Infectious material may have leaked out through inadequately stoppered tubes. The glass tube may have been broken, causing both the metal sleeve and the wooden container to become infected.
6. Protect your hands against injury during the unpacking of such shipments. Use tools to loosen tight stoppers or metal lids, otherwise you will injure your hands and infect yourself with pathogens. In case of injury, see: First Aid in Laboratory Infections.
7. Empty containers must be stored in such a manner that no one can infect himself from them. They must be subjected to suitable sterilization prior to re-use.
8. Postal shipments are governed by particularly stringent regulations. The package must be packed so as to be unbreakable; it must be tied and distinctly marked with a 'Caution' label on the outside.
9. In addition, observe the legal regulations pertaining to the shipment of pathogens, dated 21 Nov 17 - Reichs gesetzblatt page 1069, with supplements dated 17 Dec 21 - RGBl. page 1608, and 17 July 32 - RGBl. page 352. All of these are designed to prevent infection with agents of disease and epidemics, and to preclude their dissemination."

10. Letter shipments may not be dropped into mail boxes, but must be delivered to post office windows or handed to rural mail carriers.
11. Shipments of the agents of plague, cholera, tularemia, hoof and mouth disease, glanders, and hog cholera, or material suspected of harboring same, must be reported to the consignee by telephone or telegram. Receipt must be acknowledged at once. The same is valid for shipments of viable cultures."

A number of laboratories concerned with the transportation problem had developed mailing and shipping containers in the hopes of establishing uniform procedures within their countries. These were similar to specimen containers used in this country.

Figure 61, A shows a shipping container used in Germany for liquid cultures or specimens which must be refrigerated. The container will accommodate one liter of culture material. The culture is put in 250-milliliter glass bottles which are enclosed in a metal can with a slip-type top. The metal cans fit into spring-loaded holes in the base of the container and are pushed tightly against the lid when it is closed. The lower part of the insulated container contains cracked ice.

Figure 61, B shows an all-purpose specimen container used in a Swedish laboratory to insure that pathogens are not transferred from the laboratory to the hospital ward. The container is autoclaved each time it is taken out of the laboratory.

M. TUBERCLE BACILLI CULTURE TECHNIQUES

Techniques used for the detection and culture of tubercle bacilli from specimen material were observed more frequently than any other. Consideration of some of these techniques is warranted since it indicates the degree to which the laboratories were or were not concerned with the hazards arising from these procedures.

Theoretically, a good way of improving safety is to eliminate certain hazardous steps in a procedure involving infectious microorganisms. Techniques developed and used in two European laboratories eliminated hazardous steps in the detection of tubercle bacilli from sputum samples.

The following technique is employed at the Bacteriological Laboratory of the Public Health Laboratory Service at County Hall, London, England.

> Sputums are received in disposable, flat, top opening, tin cans about three inches in diameter and 3/4 inch high. About two milliliters of the specimen is added to two milliliters of soda solution in a screw-capped bottle. The tubes are shaken for 45 minutes on a Kahn shaker on the laboratory floor. The tubes are then opened in

A

B

Figure 61. Culture and Specimen Containers.
A. Refrigerated Shipping Container.
B. Hospital Specimen Container.

a ventilated cabinet and five milliliters of acid phosphate buffer solution added to neutralize. Manipulations done before culturing are considered to be of low-level risk because of the small number of infectious organisms involved. It was felt that only cultures which contain 10^7 or 10^8 cells per milliliter constitute an infectious aerosol hazard.

After neutralization, one milliliter of the digested sample is added to a screw-capped bottle containing ten milliliters of a Kirshner-type liquid medium with serum and penicillin added. The centrifugation step is eliminated, thereby avoiding those hazards attending the manipulation of screw-capped bottles in centrifuges.[39]

Tubercle bacilli grow in colonies in the liquid media. After incubation, colonies are fished out and subcultured on Lowenstein solid medium. Growth from this medium is emulsified in a Tween solution and used as inocula for sensitivity tests. This, according to scientists in this laboratory, is the most dangerous step and must be done in a cabinet.

At the State Institute for Public Health in Oslo, Norway, a method devised by Dr. Rolf Saxholm[60,61] eliminates two steps from the normal procedure used for the detection of tubercle bacilli from sputum or urine. Saxholm's procedure is as follows:

1. The specimen is added to an equal volume of a mixture containing one per cent pancreatin-N and 1.5 per cent Desogen (methylphenyl-dodecyl-trimethyl-ammonium-methosulfate) in a borate buffer at pH 9.

2. The receptacle (British universal container) is given a short shaking by hand and placed in a dark room at room temperature for 4 to 24 hours.

3. After incubation the liquid contents of the tube are mixed and used to inoculate slants of Lowenstein-Jensen medium or Tarshis' blood agar medium.

Saxholm's procedure, although not widely used outside of Norway, eliminates the necessity for mechanically shaking digesting samples and the necessity of centrifuging the sample after digestion and neutralization.

The method used in most tuberculosis laboratories, however, requires the shaking and centrifuging of the specimen. In several American laboratories a shaking device designed for mixing paint in gallon cans was used. Because of the vigorous action of the shaker, this is a particularly dangerous technique if not carried out with great care. Following the shaking period the paint can should be taken to a ventilated cabinet for opening. Of the several laboratories in which this technique was used, it was carried out in a completely safe manner only in the laboratory of Dr. Rané Dubos, the originator of the technique.

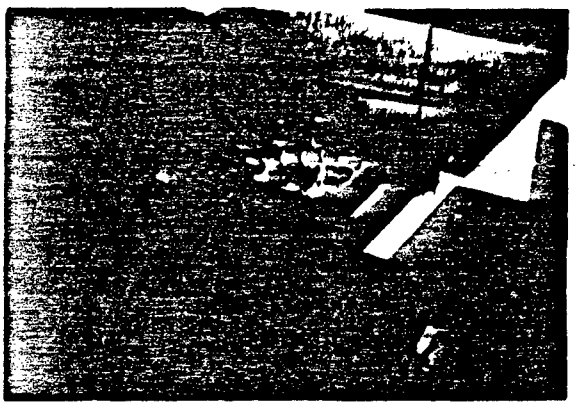
Most laboratories used a Kahn shaker or the equivalent for speeding the digestion of sputum samples. A particularly hazardous way of carrying out this technique is shown in Figure 62, A. The specimens, in cork-stoppered bottles, are on a Kahn shaker. The technician doing this operation told me that the cork stoppers were "always coming off" during the shaking procedure. Figure 62, B and C show devices used in two laboratories to prevent breakage or leakage during the shaking process. The glass culture bottles in each case had screw caps instead of cork or rubber stoppers. B shows a split form made of rubber which encases the small bottles and is clamped tightly shut before being put on the shaking machine. The metal can in C has plastic inserts with holes for the sputum bottles and pads of foam rubber for the top and bottom. The metal top for the can is not shown.

Figure 62, D shows solution bottles in a tuberculosis laboratory equipped with hooded delivery devices. The double hood device is shown schematically in Figure 63.

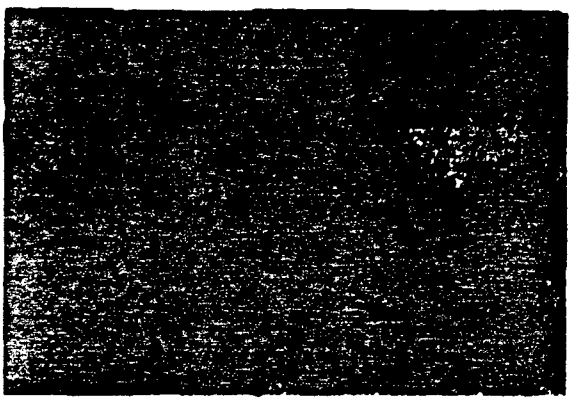
The purpose of this arrangement was to help to prevent cross-contamination between sputum bottles when digesting or neutralizing fluid is being added and to minimize contamination of the outsides of the bottles, the hands of the technicians, and the table top.

In one laboratory it was felt that pouring off the fluid from centrifuged sputum samples presented a contamination hazard. After the fluid was poured off, one drop usually was left on the lip of the bottle, and this drop frequently ran down the side of the bottle, contaminating it and the hands of the technician. To avoid this hazard, sterile decanting rods with "wiping sleeves" were made. A small piece of cotton or gauze was attached to each sterile rod just below the handle portion. When decanting, the liquid in the bottle was poured down the rod, and the cotton or gauze "tuff" was used to absorb the last drop from the lip of the bottle. The technician could merely touch the "tuff" to the lip of the bottle before discarding the decanting rod.

One hazard observed several times in tuberculosis laboratories deserves special emphasis. This involved the autopsy of guinea pigs previously inoculated with suspicious tuberculous material. Sacrificed guinea pigs before or after dissection were occasionally left on the table of the autopsy room. Two such instances are shown in Figure 64. In A, note the fly on the back of the laboratory bench. In B, the sacrificed animals had not been dissected, but flies were in the room and an electric fan on one of the table tops was operating. Apparently each morning the animal attendants sacrificed the animals and prepared them for later autopsy by the professional personnel. In the first instance the attendants partially dissected the animals and left them until the arrival of the person in charge.



A



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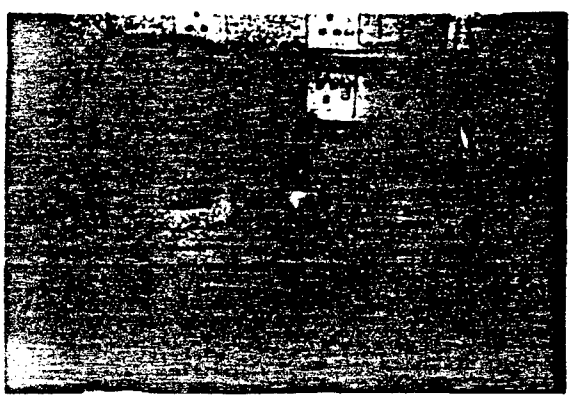


C

D

Figure 62. TB Culture Techniques.
A. Cork-Stoppered Culture Bottles on Shaking Machine.
B. Rubber Form for Culture Bottles.
C. Metal Can for Culture Bottles.
D. Hooded Solution Delivery Burettes.

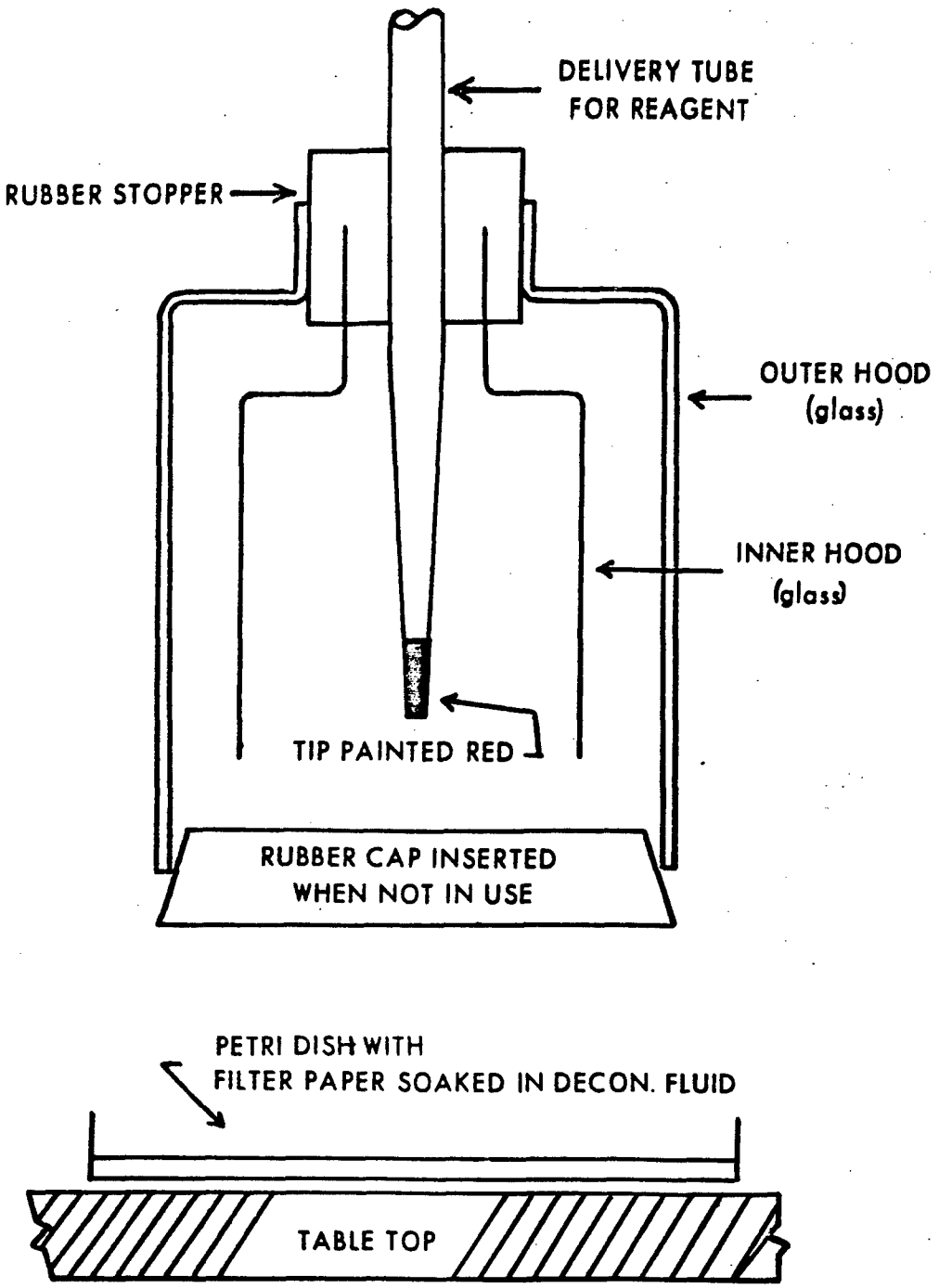
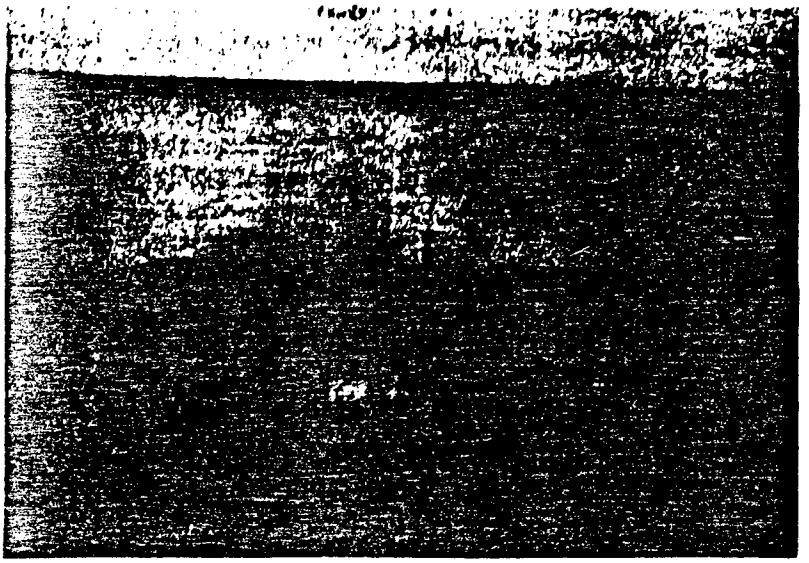


Figure 63. Double Hood Burette.



A

B

Figure 64. Autopsy of Tuberculous Guinea Pigs. A. Infectious Laboratory Bench. (Note fly circled in background.) B. Sacrificed Guinea Pigs Which Had Been Inoculated with Suspicious Material Left in Room with Flies Present and Fan Operating.

Recently, in Britain, a special working party appointed by the Medical Research Council published their recommendations of precautions which should be taken in the tuberculosis diagnostic laboratory.[40] Among the recommendations made by the committee were:

1. Separation of dangerous operations in individual rooms.
2. Ventilation of the rooms at a rate of at least six air changes per hour.
3. Installation of foot- or lever-operated sinks close to the working bench and in offices used for unpacking specimens.
4. Wearing of operating room gowns which fasten at the back.
5. Prohibition of smoking and the consumption of food or drink in infectious areas.
6. Development of sputum culture methods which avoid the use of the centrifuge.
7. Use, when necessary, of horizontal rather than angle-type centrifuges.
8. Preparation of microscopic slides without using the technique of mashing two slides together to crush selected sputum material.
9. Use of a satisfactory technique or apparatus to avoid sputtering when flaming a loop.

The committee noted that only a service-type gas mask would be useful to avoid breathing infectious aerosol, but felt that cellulose or gauze masks were of value in the autopsy room to protect against face and mouth contamination by large drops or splashes.

Unfortunately the specific recommendation of the committee regarding the use of ventilated cabinets is vague. They state that ".... it is advisable to provide a protective cabinet .... whenever more than a few cultures have to be made ...." Further, they say, "At the present time we consider that a protective hood is desirable in a laboratory handling a reasonable number of cultures and sensitivity tests, particularly when the conditions are cramped. In smaller laboratories in which only a few cultures are made, it should be possible to maintain an adequate standard of safety by other methods." Although there is no doubt that work loads affect safety standards, it is somewhat equivocable to presume that management (or mismanagement) of more than a certain number of virulent tubercle bacilli cultures would be necessary to produce laboratory infections. The cabinet recommended by the committee was that developed by Williams and Lidwell[62] and shown in this report on page 236.

A sign distributed by the British National Association for the Prevention of Tuberculosis was seen in several British and Australian tuberculosis laboratories. It read as follows:

"Remember

1. Conform to the instructions of the head of the laboratory.

2. Wash your hands after work, using soap and rinsing thoroughly. If you know your hands have been contaminated wash them in an antiseptic solution and then in soap and water before touching anything.
3. Regard your working coat as contaminated and use it only for laboratory work; never while eating.
4. Use a hooded Bunsen burner. Tuberculous material tends to 'spurt' when a wire loop containing it is flamed.
5. Have on your bench a jar containing 5 per cent Lysol and place in it any contaminated object and material no longer needed.
6. Use forceps to hold slides when fixing and staining smears of suspected tuberculous material.
7. Wear gloves when working with unfixed biopsy specimens.
8. Take great care when handling liquid cultures or other fluid preparations. Both the bench and the air can be contaminated by 'droplets'."

N. MISCELLANEOUS LABORATORY SAFETY APPARATUS

A Finnish laboratory assembled the apparatus shown in Figure 65, A to project an image of the colonies on a Petri plate onto a large frosted glass for easy counting. The rod on the right side is a focusing device. It was suggested that such an arrangement could be adapted to a closed cabinet system to simplify plate counting.

The metal containers shown in Figure 65, B, C, D, and E are typical of those used in 48 infectious disease laboratories for the discard of contaminated materials. As illustrated, several laboratory directors believed it to be important that infectious discard containers not be put directly on the floor. With few exceptions discard containers were metal and were provided with tops. However, the tops were frequently left off during the working day.

The device shown in Figure 66 was used in the change room of a Swedish laboratory. Its purpose is to keep a shoe decontamination mat constantly wet with 70 per cent alcohol.

At an American laboratory, engineers designed and built an apparatus for washing, sterilizing and drying the surface of eggs prior to inoculation with virus material. Figure 67, A shows one end of the machine, which extends through a wall to an adjoining virus laboratory. Several dozen eggs are put into metal trays in the machine from a clean room in which the candling is done. When the cycle is started, the egg surfaces are alternately washed with alcohol, dried with warm air and subjected to UV radiation. The eggs are then removed in the adjoining infectious room where eggs are inoculated.

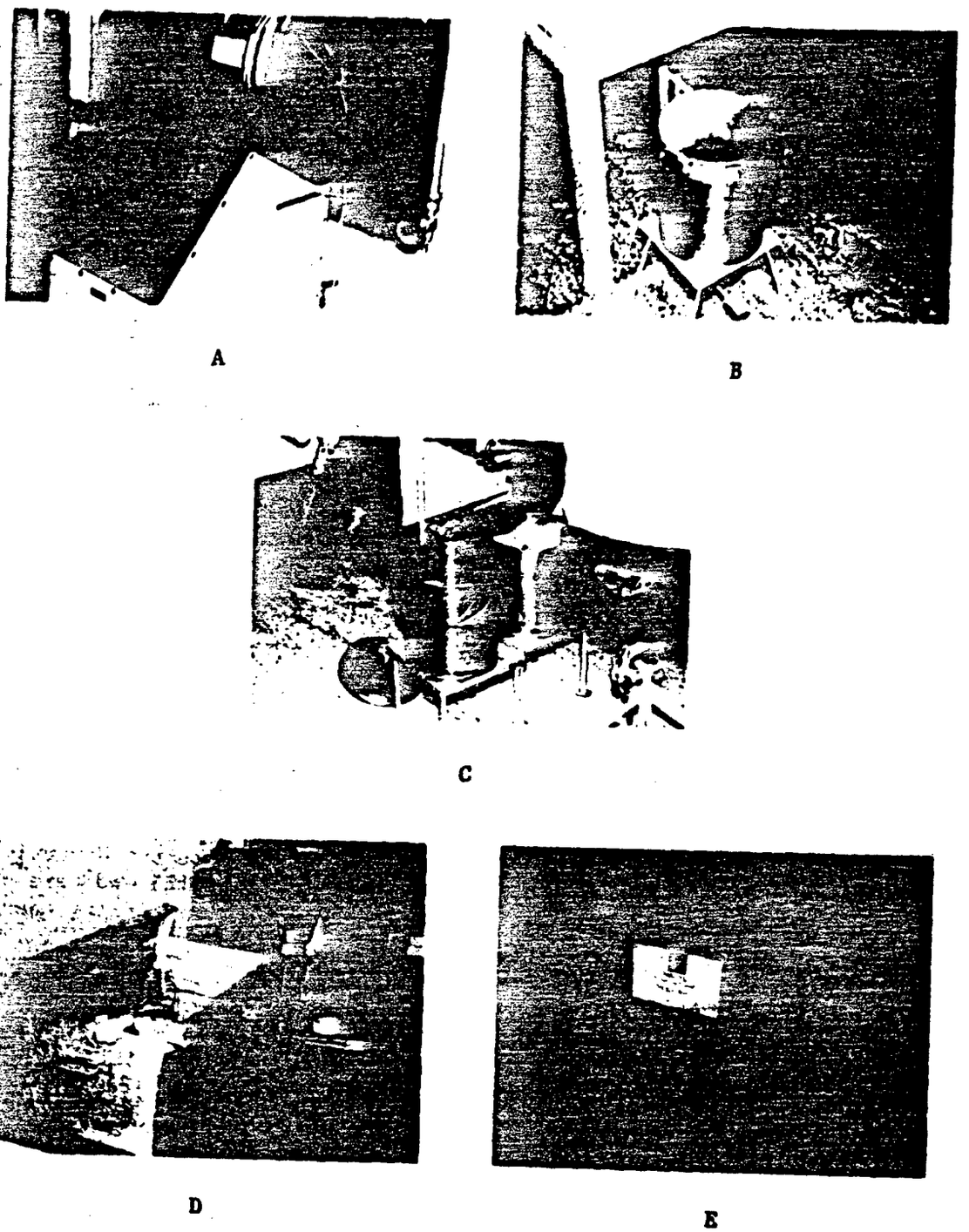


Figure 65. Miscellaneous Laboratory Apparatus.
A. Delineascope for Colony Counting.
B, C, D, and E. Discard Containers.

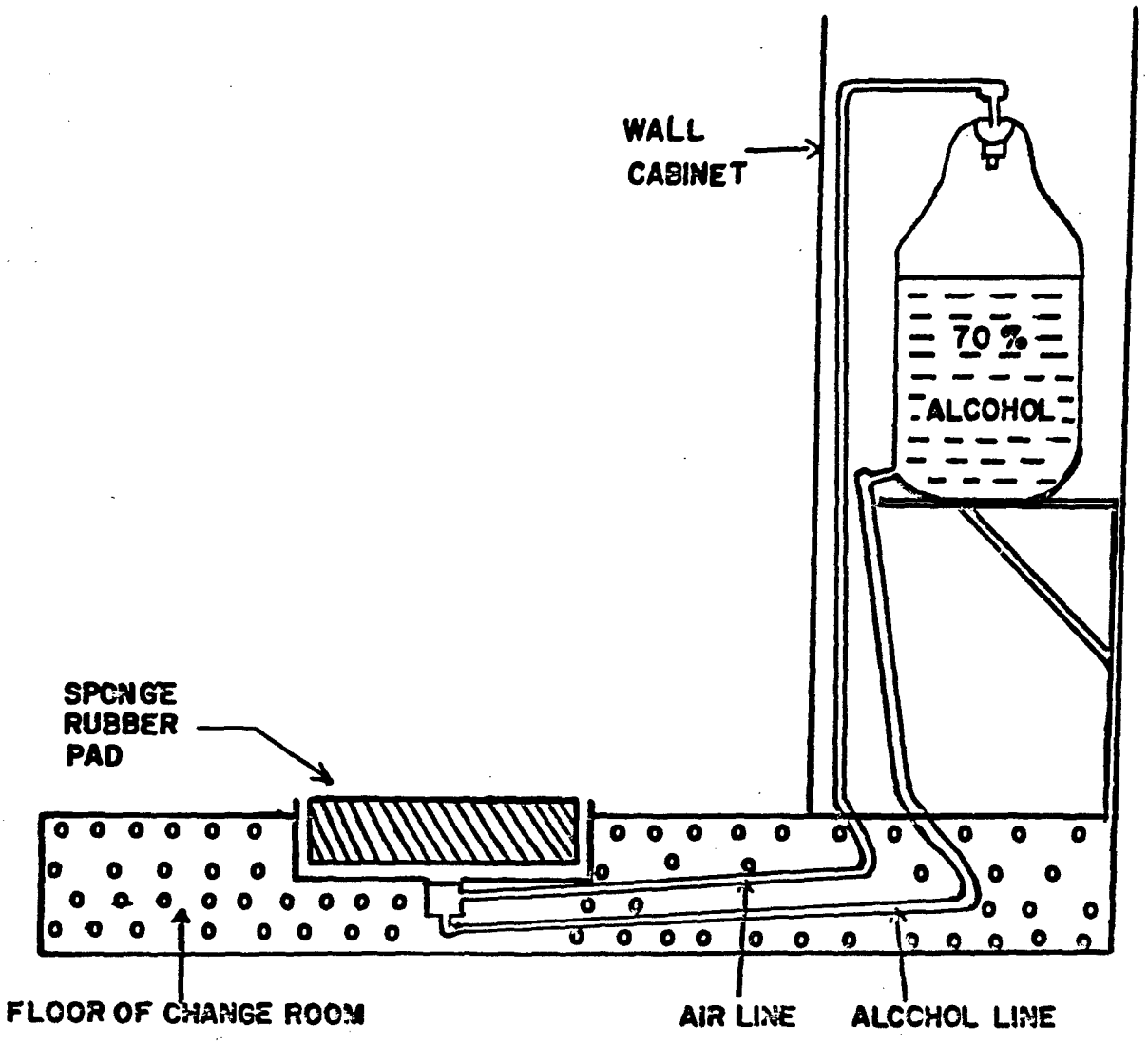
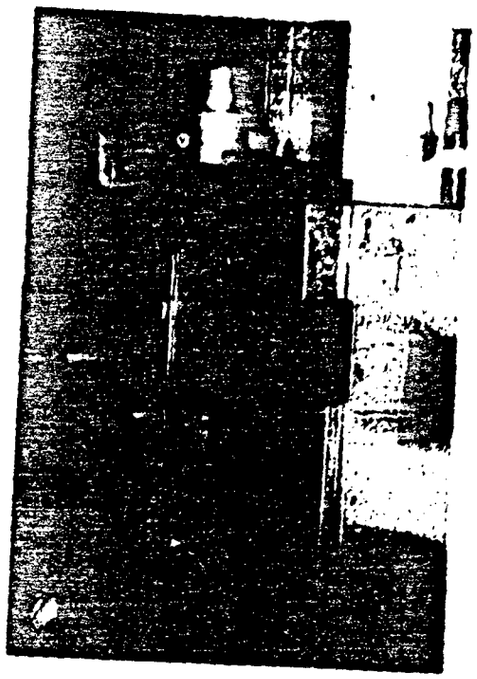


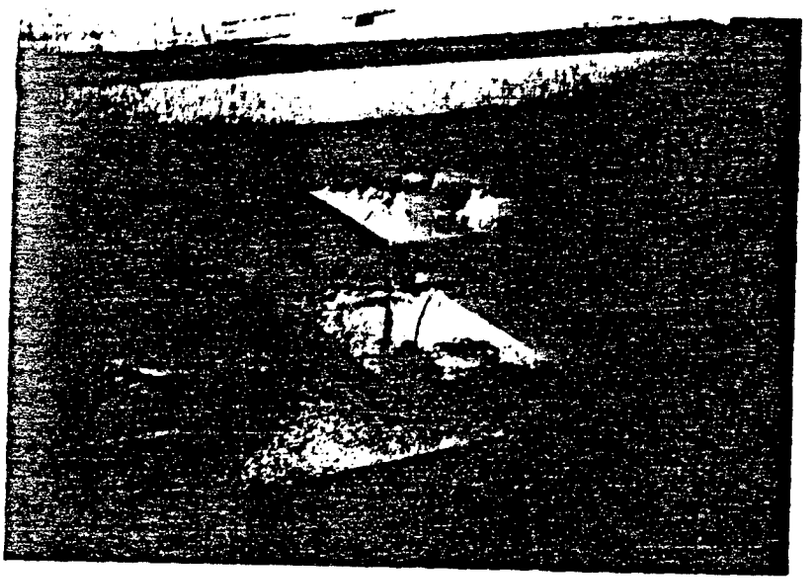
Figure 66. Disinfectant Floor Mat.



A

B

Figure 67. Apparatus for Handling and Opening Eggs.
A. Egg Sterilizing Apparatus.
B. Exhaust Device for Egg Dust.



C

D

C. Plastic Chamber for Opening Eggs.
D. Flame Device for Opening Eggs.

The breathing of the dust created when opening eggs with a grinding wheel was avoided in one laboratory with an air exhaust pipe and a plastic shield (Figure 67, B). The exhaust tube is connected to a vacuum cleaner under the table. A nonventilated egg opening device is shown in C. The flame device for opening eggs shown in D uses a 78 rpm phonograph motor to turn the platform holding the egg.

Technicians in one Finnish laboratory preferred to use foot-operated gas burners (Figure 68, A). They suggested that this type of burner be used in ventilated safety cabinets. Note the stainless steel table tops.

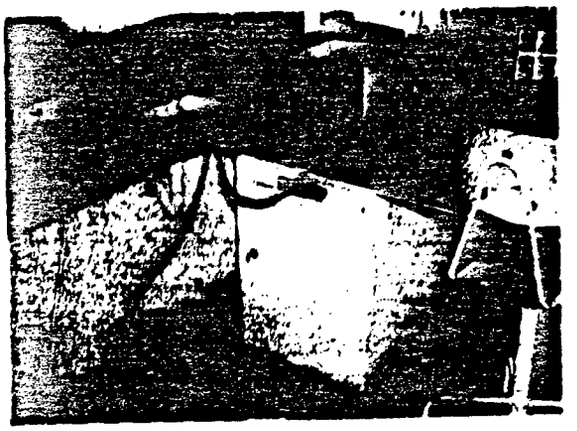
Excessive breakage of culture plates in an incubator room prompted the design of the racks shown in Figure 68, B.

In a British laboratory, plastic tubing of various sizes was found useful for enclosing contaminated material to be moved from area to area or for protecting clean items from becoming contaminated (Figure 68, C).

The metal springs shown in Figure 68, D were developed at the Microbiological Research Establishment in Porton, England. Sets of springs to accommodate flasks of varying size were used to hold them securely on a horizontal shaker.

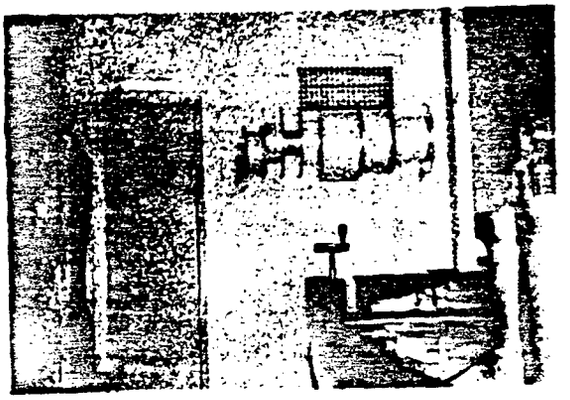
Surprisingly few safety signs or posters were seen in the laboratories visited. In some laboratories signs, regulations, or posters were not noticed although state or federal regulations required that they be posted in a conspicuous place. Safety signs were most frequently seen in tuberculosis laboratories. In one British laboratory the sign illustrated in Figure 69 was placed on the door of rooms in which infectious work was being done. Thus the name of the person in charge, the name of the infectious agent, and the protective clothing required for entrance could be quickly determined.

Closed tissue blendors were seen in seven laboratories. Figure 70 shows two views of a blendor used in several German laboratories and stated to be aerosol tight. Both the glass bottle, which contains the tissue to be macerated, and the metal cooling jacket seat on a flat rubber gasket in the mixer head.

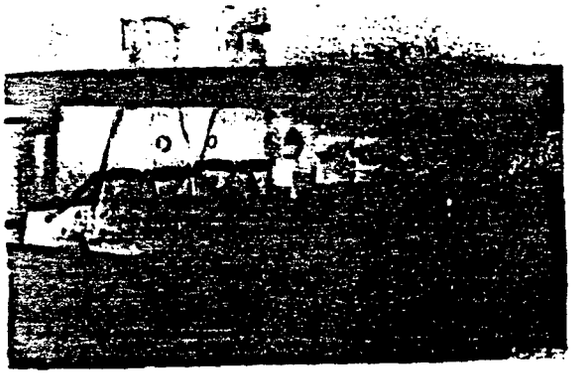


A

B



C



D

Figure 68. Miscellaneous Laboratory Apparatus.
A. Foot-Operated Gas Burner.
B. Petri Dish Racks.
C. Dispenser for Plastic Tubing.
D. Shaking Machine Springs.

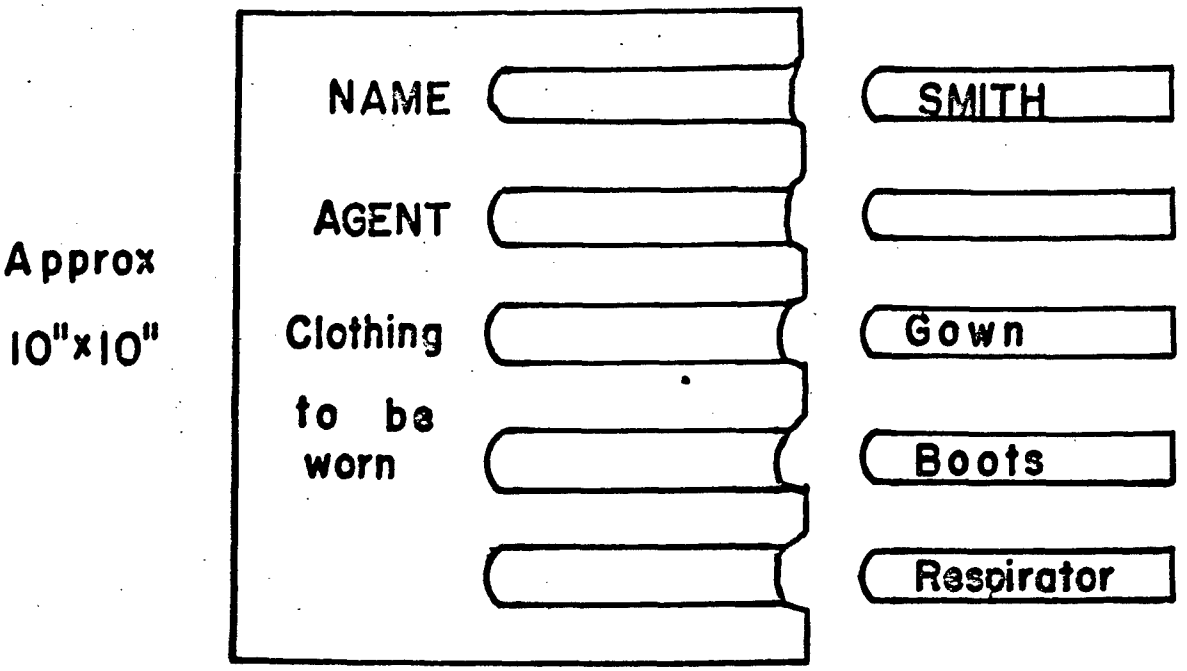


Figure 69. Safety Door Sign.

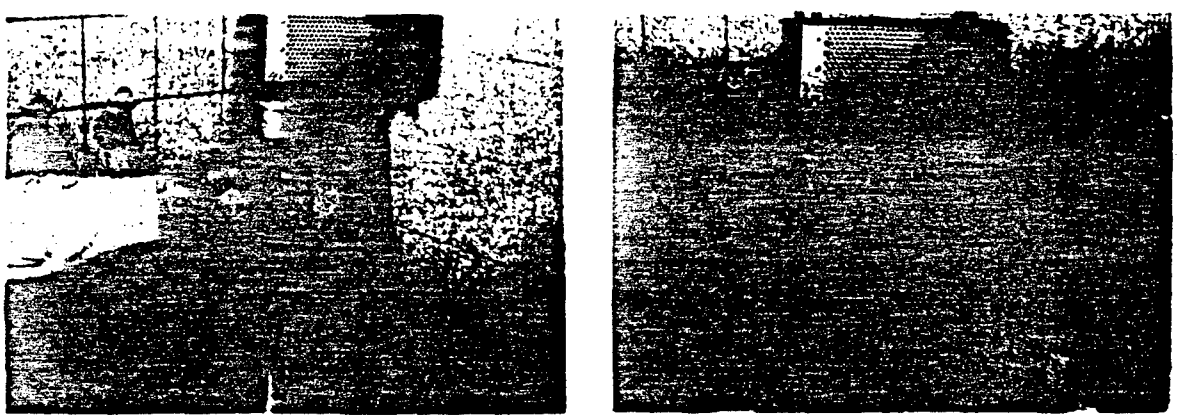


Figure 70. Closed Tissue Blendor.

VII. LABORATORY EQUIPMENT AND FACILITIES

Facilities and equipment in infectious disease laboratories related to safety and not included in Chapters V and VI are treated in this chapter. After a recapitulation of the over-all observations, the major portion of the chapter deals with animal and autopsy room equipment, laboratory safety cabinets, and germicidal ultraviolet installations.

A. OVER-ALL OBSERVATIONS

Table XXXV illustrates the frequency with which certain common apparatus was seen in the laboratories. Much of it was of German, British, or American manufacture. In general the equipment seen in commercial laboratories or in government-owned research institutions was better than that used in schools and universities.

TABLE XXXV. SOME GENERAL EQUIPMENT PRESENT IN 102 MICROBIOLOGICAL LABORATORIES

TYPE OF EQUIPMENT	PER CENT OF LABORATORIES HAVING THE EQUIPMENT
Aerosol exposure apparatus	11
Autoclaves, electric	10
Autoclaves, horizontal	75
Autoclaves, top loading	27
Centrifuge - lyophilizing apparatus	14
Continuous or large-scale culture apparatus	12
Electron microscopes	15
Electrophoresis apparatus	17
Lyophilizing apparatus	43
Sharples or DeLaval centrifuges	11
Spinco high speed centrifuges	63

Of more direct concern, is an accounting of safety equipment seen in the laboratories as shown in Table XXXVI. Many of the items listed are discussed in detail elsewhere. Not all of the equipment listed in Table XXXVI actually provides the expected degree of personnel protection. For example, in the seven laboratories which had some type of safety blendor, only one blendor was actually aerosol tight. In 38 per cent of the laboratories, safety equipment was being used which had not been properly safety tested. These are listed in Table XXXVII. In addition, ten per cent of

the laboratories had safety equipment (usually safety cabinets) available which was no longer being used. Safety devices of original design were seen in 37 per cent of the laboratories. These were usually cabinets, ventilated animal racks, or loop incinerators.

TABLE XXXVI. TYPE OF SAFETY EQUIPMENT PRESENT IN 102 MICROBIOLOGICAL LABORATORIES

TYPE OF SAFETY EQUIPMENT	PER CENT OF LABORATORIES HAVING THE EQUIPMENT
Air sampling devices	23
Animal cage rack, degastoria	5
Animal cage racks, ventilated	8
Blendors, closed type	7
Centrifuge cups, safety	12
Centrifuges, non-balance type	19
Centrifuges, Sharples or DeLaval, inclosed	5
Centrifuges, ventilated	6
Ethylene oxide chambers	7
Loop incinerators, commercially made	13
Loop incinerators, homemade	8
Lyophilizing apparatus with filter	1
Pans, covered for discard items	47
Pass through locks with ultraviolet	25
Pipette discard containers, horizontal, autoclavable	21
Pipette discard containers, upright, autoclavable	8
Pipettors (including bulbs)	51
Syringes, needle-locking	30

TABLE XXXVII. SAFETY EQUIPMENT AND FACILITIES IN 102 LABORATORIES WHICH HAD NOT BEEN "SAFETY TESTED"

TYPE	NUMBER OF LABORATORIES
Cabinets or cabinet filters	16
Ultraviolet treatment of exhaust or supply air	9
Closed tissue blendors	6
Building filter systems	5
Gas air incinerators	2
Ultraviolet treatment lyophilizer pump exhaust	1

The deficiency of safety facilities in existing infectious disease laboratory buildings was one of the most significant observations made during the study. As indicated elsewhere, over one half of the buildings were less than ten years old, and, in general, there was no over-all shortage of working space. Yet most of the buildings, both old and new, were lacking in most of the design features that are desirable for work with infectious agents. Also, of those buildings less than one year old or presently being constructed or planned, 22 per cent included only a token amount or no modern improvements for the safety of personnel.

Many directors are seeking information on laboratory design and feel that available information on this subject should be summarized and published. Often, when money is allotted for a new laboratory building, the director is told that he and his staff should work with the engineers and architects to arrive at a suitable design. Yet, too often, the organization or person who allotted the money has unrealistic estimates in mind based on factory, hospital, or office building construction costs. Also, the director frequently finds that within a limited time he must try to gather information about the features of his future laboratory and transmit these in understandable form to the engineers. The time element, the difficulty of communications, the inability to get precise engineering details, and money limitations frequently prevent the inclusion of modern facilities for safety.

Table XXXVIII lists the frequency of a number of safety features present in 102 laboratories. It is important to realize that, according to the most strict criteria, only 4.3 per cent of all laboratories in the study were considered to be entirely adequate and up-to-date in the field of microbiological safety. Laboratories in Sweden had a greater frequency of good design features for safety than any other, including those U.S. and Canadian laboratories visited.

Table XXXVIII indicates that 60 per cent of the buildings had ventilation systems. When laboratory rooms were ventilated the animal quarters frequently were not. Treatment or filtration of air entering laboratories was more frequent than treatment of exhaust air. More laboratories were maintained at a relative positive pressure than at a negative pressure. There seems to be a general feeling in virus laboratories that inlet air filtration and positive balance are necessary to carry out manipulations without contamination.

Twenty-three per cent of the laboratories had change rooms, but a common failing was the lack of any visual or physical separation of infectious disease area. Only 25 per cent of the laboratories had signs, change

rooms, locked doors, or any other means of indicating to a visitor when he was entering a potentially contaminated area. In one instance a laboratory room in which Mycobacterium tuberculosis, Bacillus anthracis, and other pathogens were handled was located in a large public office building with the laboratory doors opening on a central corridor. Even when lack of funds prevents more elaborate separation facilities, signs should be used to prevent outsiders from entering infectious areas.

TABLE XXXVIII. FREQUENCY OF SAFETY FEATURES IN 102 MICROBIOLOGICAL LABORATORIES

SAFETY FEATURE	PER CENT OF LABORATORIES HAVING FEATURE
Air filtered, inlet	24
Air filtered, outlet	15
Air treated with ultraviolet, inlet	13
Air treated with ultraviolet, outlet	6
Air balanced, positive in labs	21
Air balanced, negative in labs	19
Change rooms	23
Cubicles for isolation of work	46
Cubicles, ventilated	27
Cubicles, not ventilated	19
Sewage treatment systems	13
Speaking diaphragms	6
Ultraviolet door barriers	17
Ultraviolet air locks	27
Ultraviolet in upper air of labs	31
Ultraviolet used directly in labs	26
Ultraviolet reversible fixtures	7
Viewing windows in labs	41
Ventilating systems in buildings	60

Another observation is that less attention is given to the infectious hazards relating to the holding and autopsy of laboratory animals than to any other phase of laboratory operations. In laboratory after laboratory it could be seen that less budget money and less supervisory attention was given to the animal holding and autopsy operations than to any other phase of the laboratory operations. Indeed, autopsy and animal holding rooms were sometimes converted horse stables or coal bins.

Ultraviolet lamps were used in 74 of the 102 laboratories. While a variety of ultraviolet emitters were used, most were of the hot cathode type. Unfortunately, at 55 of these laboratories the germicidal radiations were not effective. The most frequent deficiencies were:

1. Lamps not tested or changed
2. Lamps not cleaned
3. Insufficient number of lamps used
4. Lamps turned off
5. Hot cathode lamps used in strong air streams.

In addition to filter systems and ultraviolet irradiation, two other methods of air treatment were observed. In eleven instances air from rooms or cabinets was sterilized by heat furnished either by electricity or gas.

To complete the composite picture of laboratory facilities and equipment the data gathered on microbiological safety cabinets have been assembled in Table XXXIX. Only nine of the 55 laboratories having some type of cabinet for infectious operations had cabinets that were considered efficient in all respects. Even among these only four laboratories had included facilities for sterilizing the cabinet filters before changing.

TABLE XXXIX. MICROBIOLOGICAL CABINETS IN 55 OF 102 MICROBIOLOGICAL LABORATORIES

	CABINET DESCRIPTION	NUMBER
1.	Number of laboratories having ventilated cabinets	38
	Open panel cabinets	34
	Adequately ventilated	12
	Adequate filter	17
	Ultraviolet inside	28
	Exhaust directly to outside	7
2.	Number of laboratories having nonventilated cabinets	25
	Ultraviolet inside	23
3.	Number of laboratories having fume hoods with exhaust	34

B. ANIMAL CAGES

Cages for holding infected animals were constructed from a variety of materials, as indicated in Table XL. In a significant number of laboratories there had been little or no change in equipment or methods of animal care for several decades.

TABLE XL. TYPES OF ANIMAL CAGES IN 90 LABORATORIES

CAGE MATERIAL	RELATIVE FREQUENCY
Galvanized steel	71
Stainless steel	46
Wood	29
Glass	21
Plastic	3
Clay (pottery)	1
Concrete	1

Figure 71, A illustrates pottery cages used to hold tuberculous guinea pigs. The light colored cages had been recently purchased. These cages are heavy, will not withstand steam sterilization, and are easily broken. B shows heavy glass museum jars being used as cages for tuberculous guinea pigs. Cages are not changed or cleaned during the six-week holding period, but periodically fresh hay for bedding is placed on top of the old bedding. Odor control becomes a problem under these conditions as the material in the lower part of the cage begins to putrefy. Excess moisture and other factors proscribe a healthy environment for the animals. These cages are easily broken, and cannot be autoclaved.

Figure 71, C shows glass cages housing mice inoculated with Russian spring-summer encephalitis virus. Note that the cage racks in this room are also used for storage of materials and equipment. The cages were not autoclaved after use. D shows stationary metal cages for infected animals. These are impossible to sterilize and difficult to disinfect. E illustrates galvanized metal cages containing infected mice. The cages are closely spaced on wooden shelves. Note the escaped (infected?) mouse in the center of the picture. The rough edges of the cage tops present an additional hazard to workers in this room. F shows modern stainless steel cages in a recently constructed laboratory building.

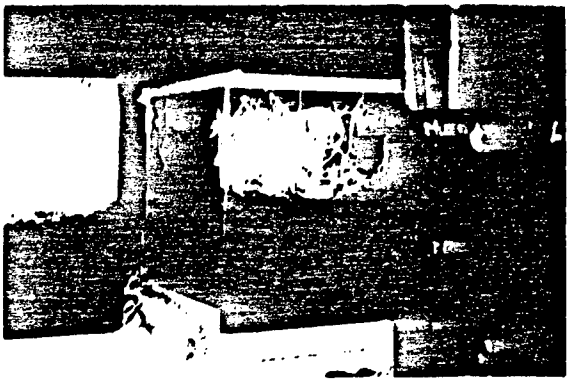
In one large British laboratory all animal holding cages were made so that they could be disassembled for storage. Anodized aluminum trays served as the cage bottoms. The sides of the cages are formed by sliding together four sheets of aluminum having their edges shaped as shown in Figure 72.

C. ANIMAL CAGE RACKS

1. Nonventilated

Racks for holding animal cages were made of a variety of materials including galvanized steel, aluminum, stainless steel, wood, and concrete. In a number of laboratories, including some which were recently built, cage

A



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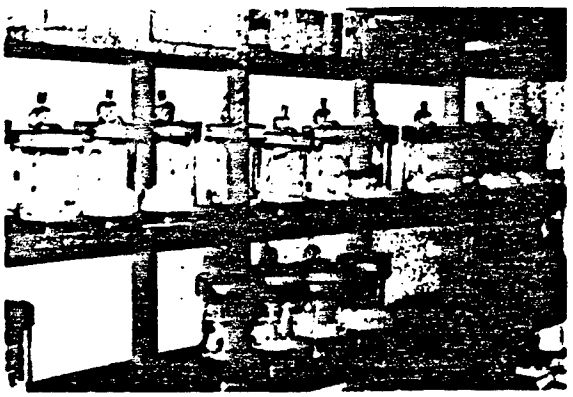

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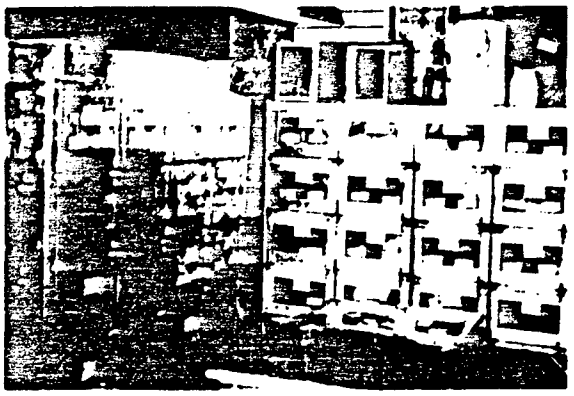

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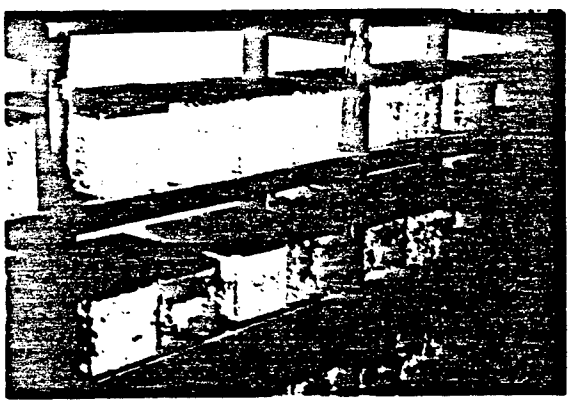
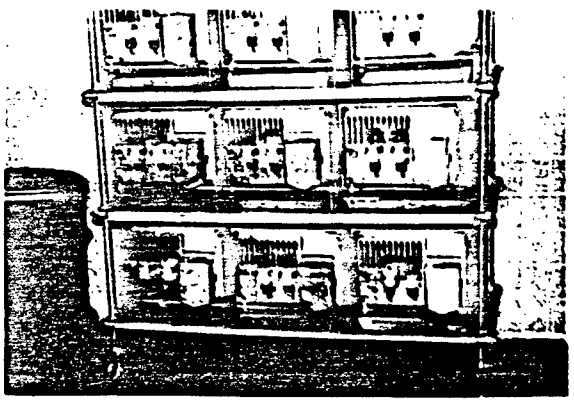


E



F

Figure 71. Animal Cages.
A. Pottery Cages.
B. Heavy Glass Cages.
C. Glass Cages.
D. Stationary Cages.
E. Galvanized Metal Cages.
F. Stainless Steel Cages.

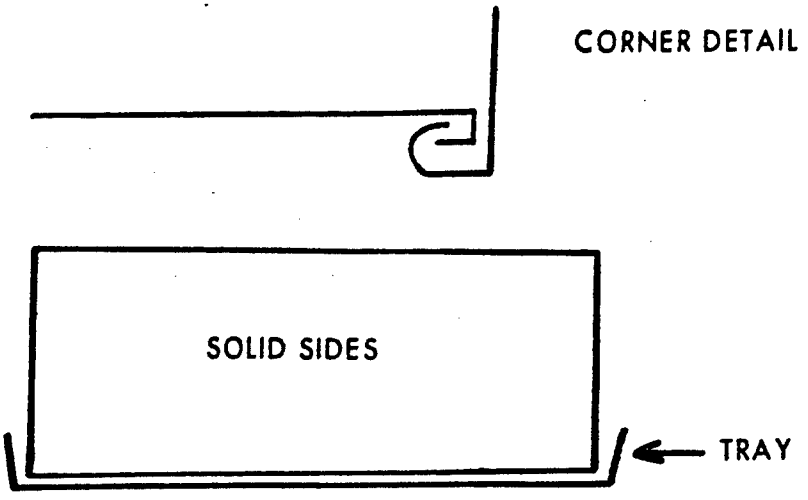


Figure 72. Details of Collapsible Animal Cages.

racks in infectious animal rooms were made of wood. These were usually permanently attached to the wall and difficult to decontaminate. Modern laboratories often were equipped with metal cage racks on wheels or suspended from the ceiling. Racks of these types simplify the cleaning and decontamination of animal rooms.

In relation to animal room hygiene and safety, and in view of existing ventilation rates and temperatures, the design and placement of animal racks in a number of laboratories created problems with overcrowding and animal cross infection. In 34 of 90 laboratories known instances of animal cross infection were mentioned. I judged the facilities at only four existing buildings to be sufficient to prevent all animal cross infection. In no instances were ultraviolet lamps used on animal cage racks to prevent animal cross infection.[63] Too often, cage racks in infectious animal rooms were used to store feed, water bottles, or laboratory instruments and equipment.

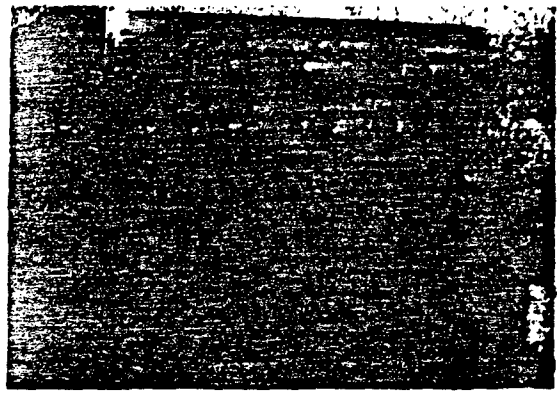
Some representative types of nonventilated animal cage racks are shown in Figure 73.

In one Scandinavian laboratory sliding animal cage racks were used to conserve space. Shown in Figure 73, C, these racks could be moved apart at any place to provide a temporary aisle for feeding and watering. In my opinion this is not a desirable technique because dust is raised each time a rack holding animal cages is moved.

2. Ventilated

In 16 laboratories infected animals were kept in some type of ventilated caging device. In most instances the racks were used to house animals infected with Mycobacterium tuberculosis.

A



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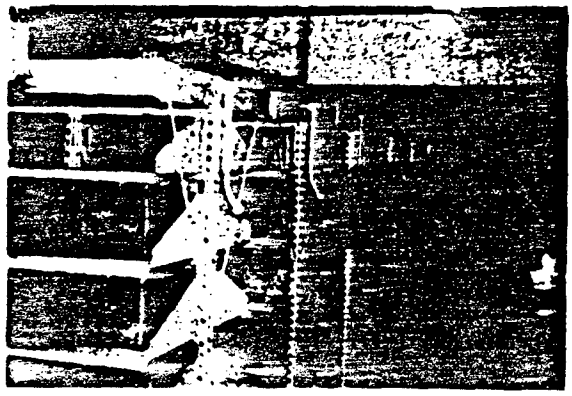


C

D

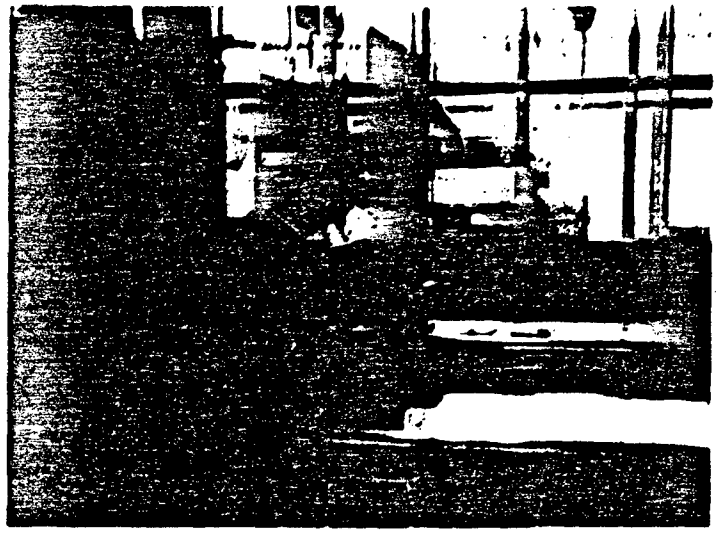
Figure 73. Nonventilated Cage Racks.
A. In a TB Animal Room.
B. Mouse Breeding Cage Rack.
C. Sliding Cage Racks.
D. Stationary Cage Racks.with Water Washing Trough.

At the Imperial Chemical Industries laboratories at Alderley Park, Macclesfield, England, all tuberculous animals were held in "ventilated cupboards" as shown in Figure 74, A. Animal cages were put into the system through all-glass flap-doors. The exhaust is arranged so that there is an automatic increase of exhaust air when a flap-door is opened. A conveyor at the lower level is used to transport cages to and from the ventilated cabinet at the center of the system. In the cabinet animals are injected, fed, and examined. Dead or sacrificed animals are taken to another ventilated cabinet for autopsy. Air enters these ventilated cupboards through louvers in the wall near the floor and is exhausted at the top. The louvers are designed to allow a high rate of air change without creating drafts. They may also be dismantled and sterilized. Air leaving the animal cupboard passes through bacteriological filters in the attic. Duplicate exhaust systems are provided so that one may be isolated for in situ sterilization while the other is in use.

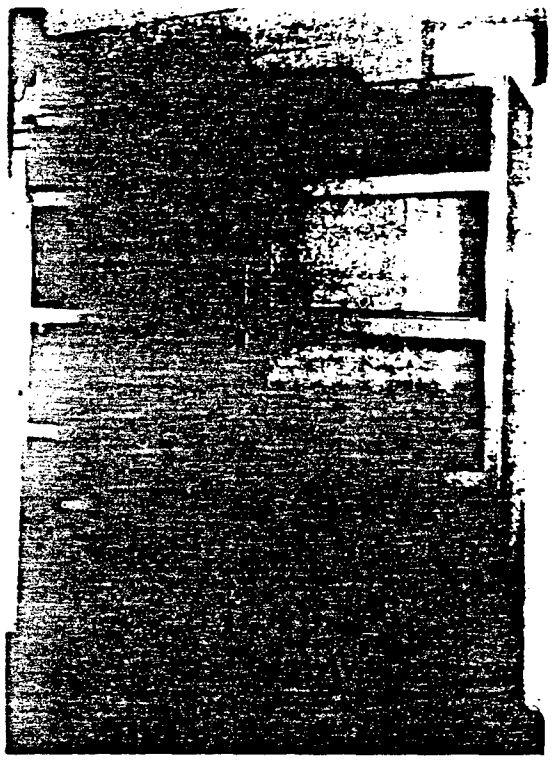
A somewhat similar, although less elaborate, cage system was inspected at the laboratories of the National Institute for Medical Research at Mill Hill in London. Used exclusively for tuberculosis infected animals, the cage racks resembled bookshelves with sliding glass doors. As seen in Figure 74, B, they have exhaust ducts at the top and air inlet louvers at the bottom. The shelving is of stainless steel rods. The bottom section of the cupboard is a tank which is kept filled with Lysol solution and empties to the building drain system. The ventilation rate is such that an inward flow of between 50 and 100 linear feet per minute is maintained when all doors are open. Exhaust air goes to a central plenum chamber where it is treated with ultraviolet radiation. Figure 74, C shows two stainless steel ventilated compartments with refrigerator-type glass doors used in a U.S. laboratory for housing rabbits challenged with monkey B-virus. Air from this unit is incinerated.

At the Rockefeller Institute in New York City, I examined the ventilated animal cage units originally devised by Horsfall and Bauer.[64] These units provide individual ventilation for permanently mounted cages. Air withdrawn from the unit is incinerated. These were among the first ventilated cages used in this country.

In Sweden, several laboratories were using or planning to use a ventilated cage rack system devised by Dr. Arne Lind of Gothenburg.[65] This system is shown schematically in Figure 75. Each cage fits into a separate ventilated compartment by lifting a sliding plastic door. Air enters each ventilated compartment through a small gap at the top of the sliding door at a velocity of 80 linear feet per minute. Rather than going directly into the cage, the air sweeps over the top of the cage causing eddy currents which gradually change the air in the cage. Air is exhausted through a channel at the rear of the cage rack system. Cardboard cages 11 by 15 by 18 inches are impregnated with copper naphtenate and copper pentachlorophenate to prevent gnawing by guinea pigs. The cardboard includes a layer of asphalt-treated paper to reduce moisture penetration. Metal cages must be used for rabbits. Each cage will hold three guinea pigs and is not cleaned or changed during a six-week holding period. Additional wood shavings, however, are added regularly.



A



B

C

Figure 74. Ventilated Animal Cage Racks.
A and B. Ventilated Systems for TB Animals.
C. Ventilated Cage Rack for B-Virus Animals.

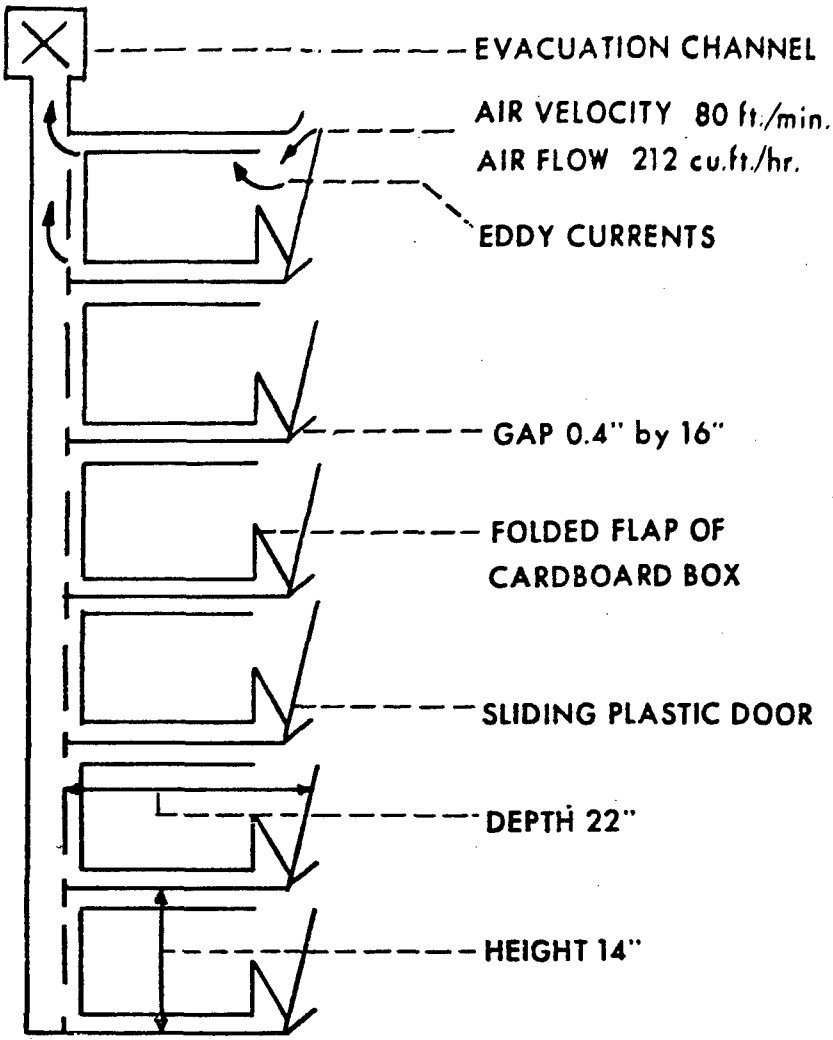


Figure 75. Ventilated Cage Rack System of Lind.

In the first units built and tested by Dr. Lind in Gothenburg (Figure 76, A) a total of 192 compartments were located within an average-size animal room. To test these units 105 rabbits were infected by whole-body exposure to aerosols of tubercle bacilli and placed in cages in the ventilated compartments for 3 to 90 days. Twelve normal guinea pigs were placed in open cages on the floor of the room for the 90-day period. During this time they multiplied to 33. Thirty days after the end of the holding period one of the 33 guinea pigs was found to have pulmonary tuberculosis. While this system offers a considerable degree of isolation, it is evident then that it does not provide full protection from the escape of infectious microorganisms. Probably the weakest point in the system is the necessity

of opening the plastic sliding doors in order to feed and water the animals and insert or remove cages. Exhaust air from the test installation in Gothenburg was not treated. In the new institution being built in this city some 1200 ventilated animal compartments will be provided, approximately 180 compartments per 250 square feet of animal room area.

Ventilated animal compartments of the Lind type were also seen at the Central Bacteriological Laboratory of the Karolinska Hospital (Figure 76, B) and at the Bacteriology Department laboratories of Karolinska Institute (Figure 76, C). In the former, exhaust air was treated with ultraviolet radiation, while in the latter a filter system was used.

Perhaps the oldest type of ventilated animal cage rack was that in use at the Paul Ehrlich Institute in Frankfurt, Germany. This cabinet, shown in Figure 77, A, is one of several at the Institute that is over 40 years old. Such cabinets called "Degastoria" were also seen in several other German and Italian laboratories. Their original purpose was to control the odors from animals kept in the laboratories and to prevent animals from freezing in the unheated laboratory rooms. Figure 77, B shows a modern version of the animal cabinet at the Institute of Infectious and Tropical Medicine in Munich, Germany, which is actually a constant temperature box for maintaining suckling mice. At the Robert Koch Institute, ventilated animal cabinets of this type with exhaust air filters are used for virus infected animals. "Degastoria" were also used at the Instituto Superiore di Sanita in Rome.

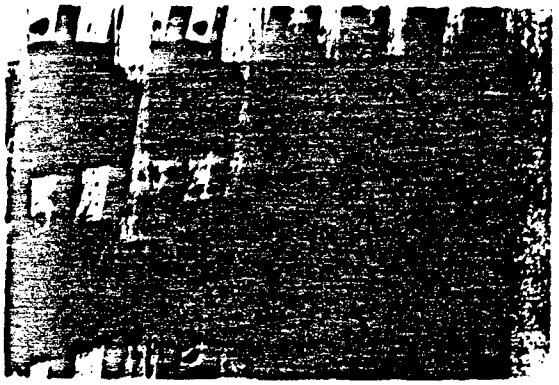
D. AUTOPSY AND ANIMAL ROOM EQUIPMENT

1. Autopsy Shields and Cabinets

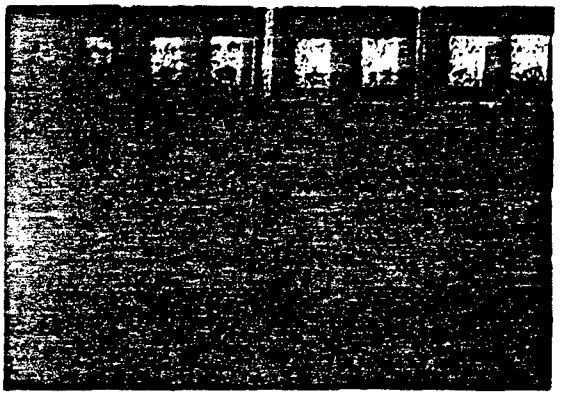
Glass shields were used in about ten per cent of the laboratories to provide barriers between the workers and animals being autopsied or eggs being inoculated or harvested. While these are helpful in preventing direct contamination of the worker by spattering of infectious materials, they do little to reduce the aerosol hazard. Shields should not be used, as they sometimes were, as a substitute for ventilated safety cabinets.

Figure 78 shows representative types of shields used in the laboratories. The one shown in 78, A was used for autopsying mice infected with Toxoplasmosis, while those shown in 78, B and C were used when opening of virus-infected eggs. 78, D shows a flat glass shield which was used during the autopsy of guinea pigs.

While many of the ventilated safety cabinets shown elsewhere in this report were used, on occasion, for the autopsy of animals, several laboratories used specially designed cabinets for this purpose. A double-sided, all aluminum ventilated autopsy cabinet used at the Imperial Chemical Industries laboratories in England is shown in Figure 79, A. It is used with attached eight-inch diameter, arm-length gloves. Materials are introduced through the ultraviolet air lock which has interlocking doors. Valves and utility outlets are located inside of the cabinet at eye-level.



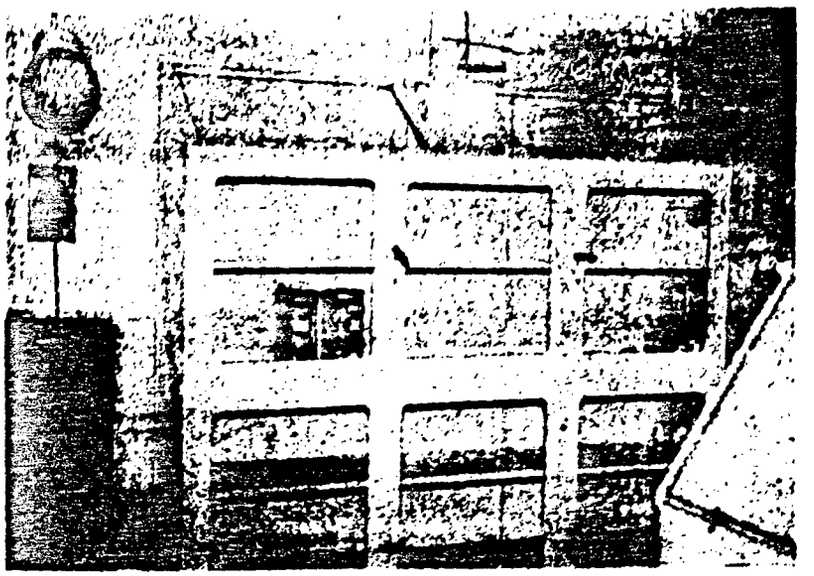
A



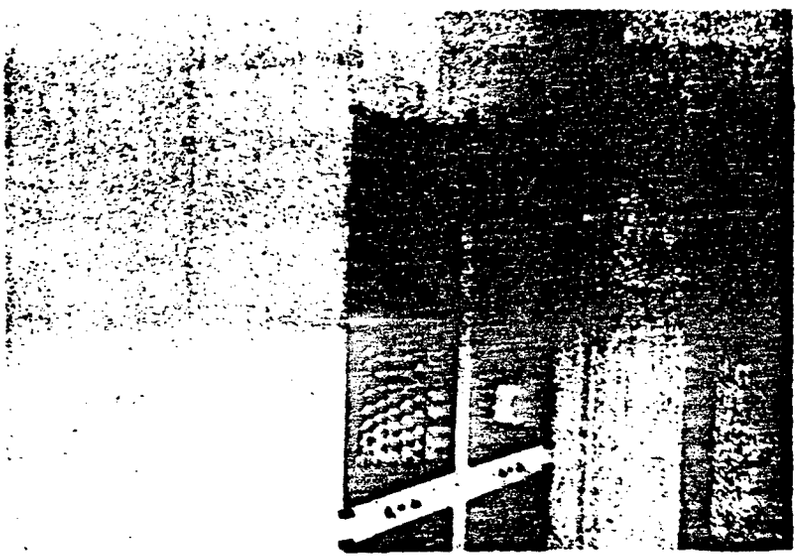
B

C

Figure 76. Ventilated Cage Racks in Sweden.
A. Prototype in Gothenburg.
B. Prototype in Stockholm.
C. Aluminum Rack in Stockholm.

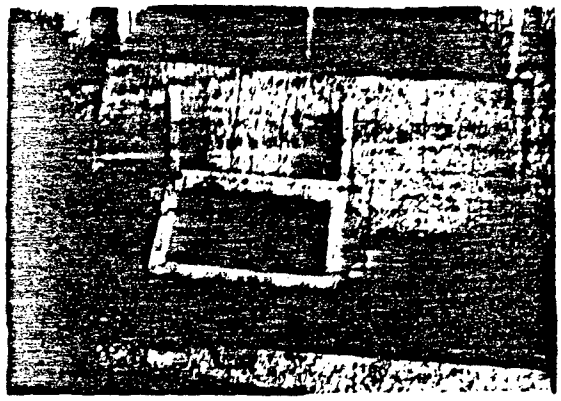


A

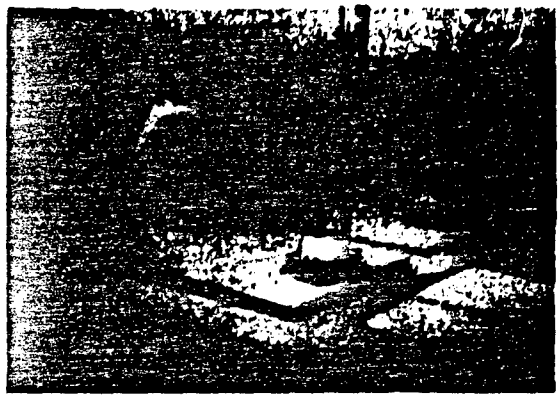


B

Figure 77. Ventilated Cage Racks in Germany.
A. In Frankfurt.
B. In Munich.



A



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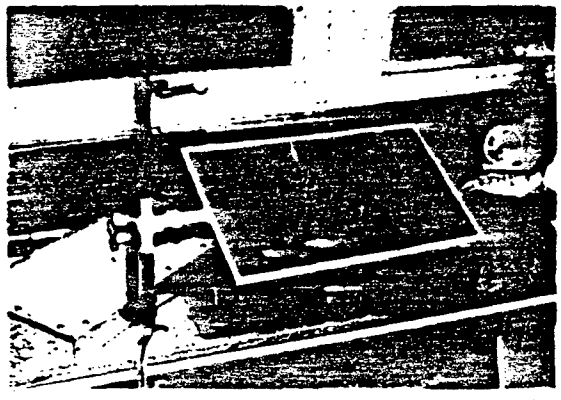

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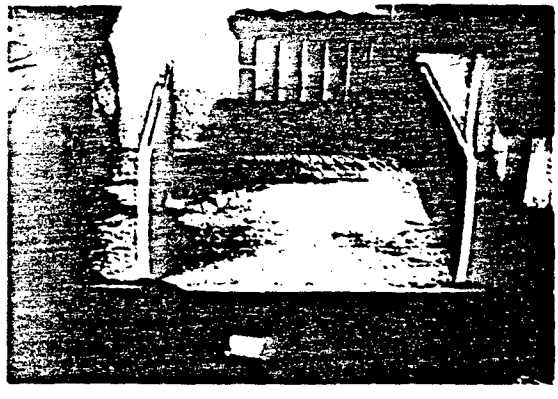


D

Figure 78. Protective Shields Used for Laboratory Work.
A. Mouse Autopsy Shield.
B and C. Egg Harvesting Shields.
D. Guinea Pig Autopsy Shield.

A ventilated cabinet for necropsy of tuberculosis infected mice developed at the National Institute for Medical Research in London is shown in Figure 79, B and C.[66] Mice are pinned to one of two revolving cork platforms. After the necropsies the cork platforms and the mice are lowered into a bath of disinfectant solution (Figure 79, C). The hinged viewing panel may be opened after decontamination with ultraviolet radiation. Air exhausted from the cabinet goes to a central plenum where it is exposed to high intensity ultraviolet radiation.

2. Miscellaneous Equipment

Some miscellaneous equipment used in animal quarters is shown in Figure 80. In several laboratories infected animals were held in wire-bottom cages with a paper lined shelf below to catch the droppings (Figure 80, A). The stainless steel box shown in this photograph was used in one U.S. laboratory to provide a means of disposing of the paper-lined shelves and animal droppings. Shelves and paper are placed in this container, which then is closed and autoclaved.

Several British laboratories employed vapors of hexyl resorcinol in animal rooms (Figure 80, B). In this picture a small vaporizer is shown on the wall of a mouse breeding room.

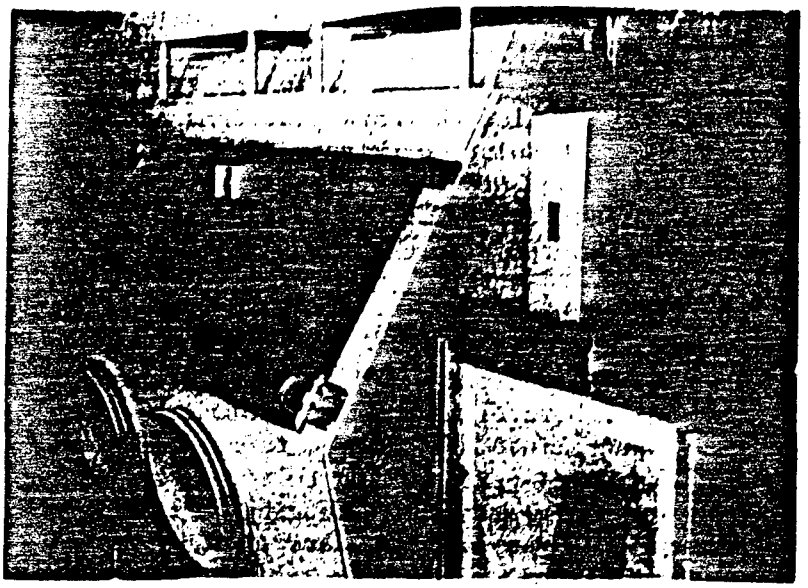
Boiling vats for animal cages were used in ten laboratories (Figure 80, C). Because most laboratories (67 per cent) do not autoclave infectious animal cages, decontamination with boiling water is better than no treatment. The disadvantage of the boiling vat, which is heated by live steam, is that the infectious debris must be removed from each cage before it is put in the vat.

Figure 80, D shows a steam generator made for degreasing automobile engines which was used to decontaminate cages. Again the debris must be removed from the cage before it is treated. 80, E is a steam jacketed boiling vat used in one laboratory to disinfect the cadavers of monkeys dead from poliomyelitis. Several other methods (autoclaving or incineration) would be preferable. A monkey autopsy table equipped with a water wash system and an air exhaust system is shown in 80, F.

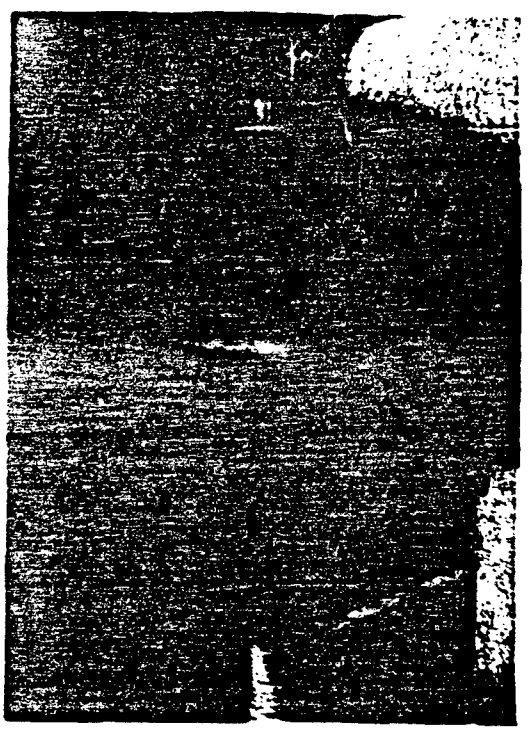
Figure 81 shows several items of protective clothing being considered for use by one laboratory to prevent animal handlers from being bitten by monkeys.

E. SAFETY CABINETS

Microbiologists have long realized the need in infectious operations for equipment to externalize hazardous procedures and manipulations. Safety hoods were in use in German laboratories as early as 1919.[67] Today the picture presented in regard to the use of cabinets is varied. In earlier days they were undoubtedly designed (and even constructed) by scientists who



A



B C

Figure 79. Ventilated Animal Autopsy Cabinets.
A. Aluminum Cabinet with Air Lock.
B and C. Mouse Autopsy Cabinet.

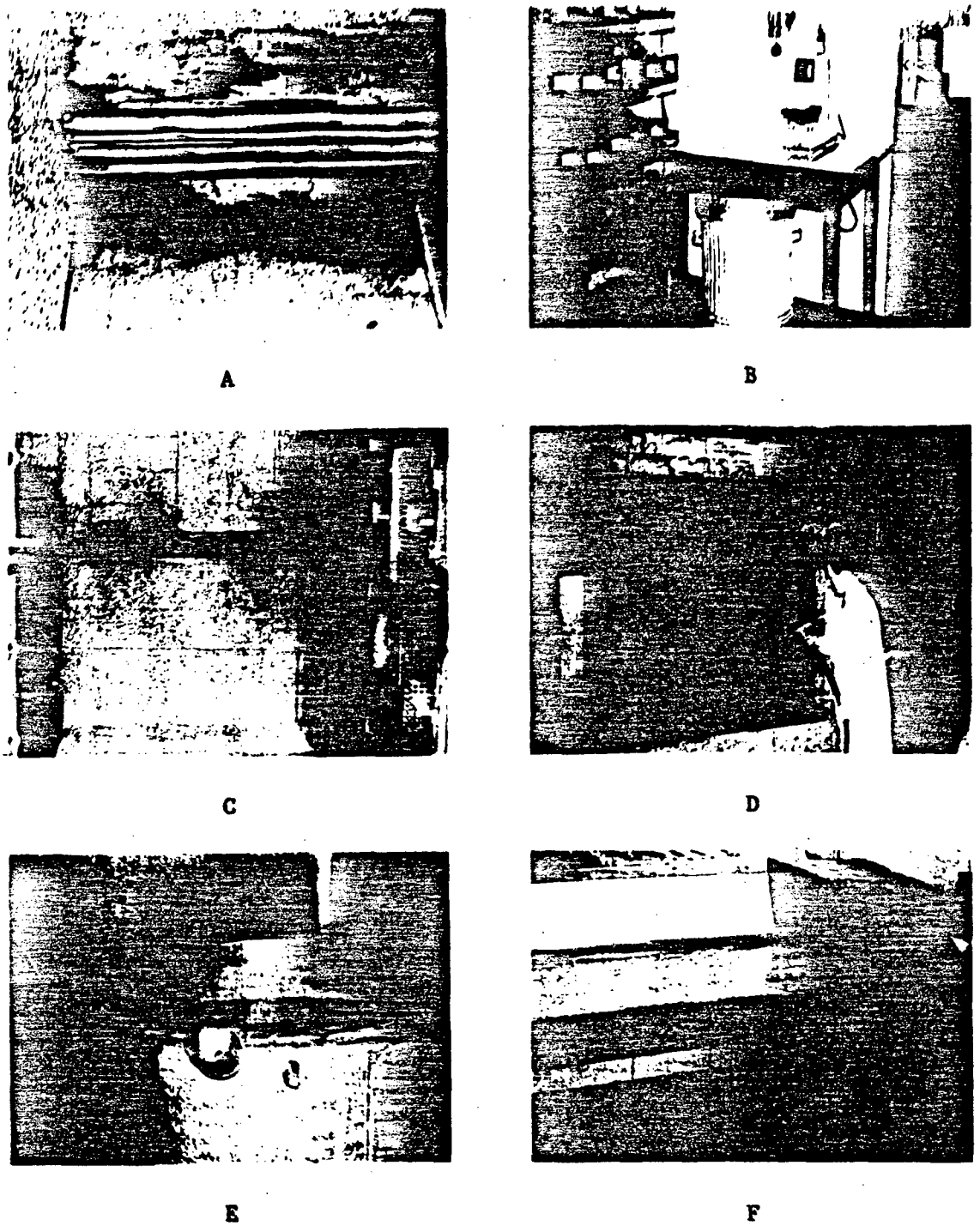
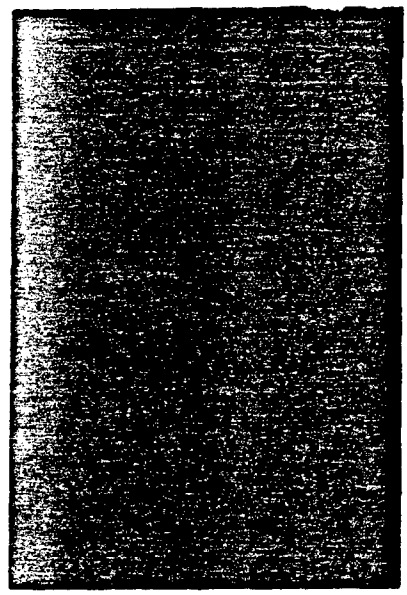
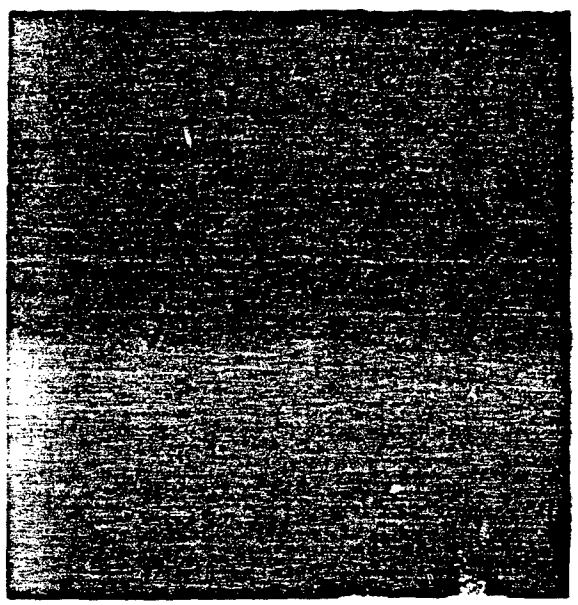


Figure 80. Miscellaneous Animal Room Equipment.
A. Box for Disposal of Paper Lined Shelves.
B. Hexyl Resorcinol Vaporizer.
C. Cage Boiling Vat.
D. Cage Steaming Device.
E. Monkey Cadaver Boiling Vat.
F. Autopsy Table with Wash Water and Air Exhaust.



A



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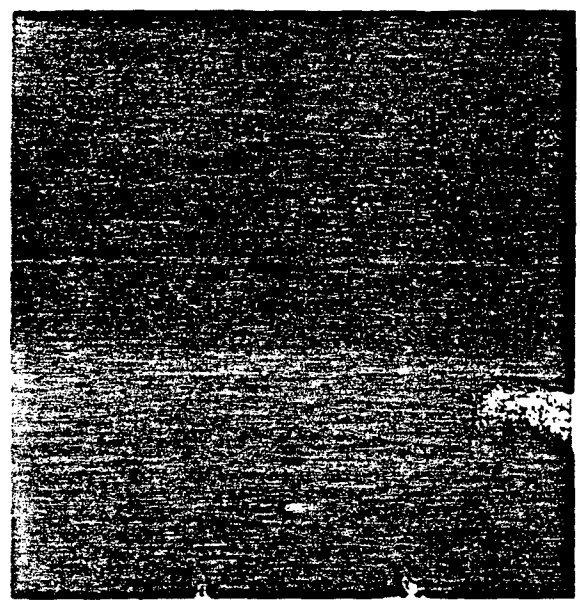


C

Figure 81. Animal Room Personnel Protective Equipment.
A. Padded Plastic Suit by the Safety Supply Co. of Toronto, Canada.
B. Two-Piece Suit of Chain Mail Made by the Whiting and Davis Company of Plainville, Massachusetts. Not shown is a pair of chain mail gloves used with the suit.
C. Reinforced Plastic Face Shield.

recognized the need for the protective devices in their own laboratories. As the need is more widely recognized and understood today, and as facilities have expanded, the tendency has been toward commercially produced equipment. However, irrespective of the source, the most important consideration is efficiency of function. Does the cabinet provide the protection for personnel or product which was intended?

Although a number of different designs and construction materials are suitable for microbiological safety cabinets, certain general criteria are essential:

1. Internal cabinet surfaces must be resistant to chemical corrosion and free of cracks or crevices which interfere with decontamination. Stainless steel is probably the most suitable, but other metals, plastics, or wood coated with a resistant finish may also be used. A glass or plastic viewing panel must be provided between the operator and the operation.

2. Sufficient inward air flow or negative pressure must be provided to prevent escape of air-borne particulates created by the procedures carried out in the cabinet.

3. An efficient air filter or air incinerating device must be used to remove or destroy air-borne microorganisms in the exhaust air stream.

4. Decontamination or sterilization of the cabinet and its air treatment device should be possible.

5. Working space in the cabinet should be ample for convenient handling of the materials used during a given procedure. Adequate working area minimizes the need for removing contaminated materials before the completion of an experiment.

6. A front panel containing ports for arm-length gloves should be available for use during work of a highly hazardous nature. The panel also provides a means of closing the cabinet for decontamination.

7. If the nature of the infectious work requires the use of arm-length gloves, a pass-through box or air lock should be attached to the cabinet. This allows passage of materials in or out when the interior of the cabinet is contaminated. Ultraviolet lamps should be put in the air lock to prevent escape of infected air.

In 1945 Shepard, May, and Topping[68] at the National Institutes of Health developed a wooden cabinet for hazardous operations such as tissue grinding and centrifuging. The cabinet was similar to a chemical fume hood. Air was exhausted through a stack in the top which contained a gas burner to incinerate particles in the air at 500°F. The natural draft from the burner provided the inward flow of air into the cabinet. In the same year the use of special cabinets similar to a design previously reported by

Van den Ende[69] were used during large-scale production of Scrub Typhus vaccine in England. These inoculation cabinets were exhausted at the rate of 50 cubic feet per minute to an electric furnace where the air was heated to 300° to 600°C before discharge to the outside. Similar cabinets were also used to house tissue fragmentation apparatus.

The use of a stainless steel cabinet for experiments with Coccidioides immitis and other infectious fungi at Johns Hopkins Hospital was reported in 1946.[70] This cabinet had a glass front and top, and a spun glass filter in the back, but no forced ventilation.

The first stainless steel cabinet meeting the design criteria given above was designed, constructed, and installed at the Biological Laboratories in 1948. Standard drawings and specifications prepared by the U.S. Army Chemical Corps were subsequently used for the purchase of cabinets of this design from the S. Blickman Co., Weehawken, New Jersey. This cabinet is often referred to as the "Blickman" cabinet. It was first described in the literature by Wedum in 1953.[57] Tests at an inward air flow rate of 50 linear feet per minute showed efficient containment of air-borne organisms within the cabinet. Other types of safety cabinets developed at the Biological Laboratories have been described by Reitman and Wedum,[71] Phillips, et al,[72] Blickman and Lanahan,[73] and Gremillion.[74] The latest described by Gremillion,[74] has been the development of completely closed, gas-tight, modular cabinet systems in which laboratory operations of an unusually high risk can be conducted safely. These systems provide containment during all manipulations of infectious materials during a laboratory experiment.

A number of publications from the Biological Laboratories have described methods of filtering or incinerating air removed from microbiological safety cabinets.[75-78]

In England, in 1957, Williams and Lidwell[62] conducted experiments in an open-panel ventilated cabinet to determine the efficiency of aerosol containment and removal by ventilation and ultraviolet irradiation. Aerosols of Bacillus subtilis spores, dried on talc, or Serratia marcescens were produced in test cabinets while air was sampled at a point 12 inches in front of the cabinet opening. Results of four experiments with B. subtilis spores are shown in Table XLI.

Ventilation rates of 50 to 60 linear feet per minute prevented the escape from the cabinets of 98.8 to 99.3 per cent of the air-borne cloud, while efficiencies for an inward air flow of 100 linear feet per minute were between 98.7 and 99.93 per cent. In one test at 100 linear feet per minute, simultaneous irradiation of the interior of the cabinet did not increase the efficiency of aerosol dispersal. These investigators felt that a cabinet ventilation rate of 100 linear feet per minute should be specified to provide a sufficient margin of safety. They observed that movement of the hands in one cabinet during testing increased the amount of aerosol escaping from the open panel.

TABLE XLI. EFFECT OF VENTILATION AND UV IRRADIATION IN PREVENTING THE ESCAPE OF AIR-BORNE BACTERIAL SPORES FROM BACTERIOLOGICAL CABINETS[a]

CABINET CONDITION	COLONIES COLLECTED OUTSIDE THE CABINET[b]	REMOVAL EFFICIENCY[c]
Test 1		
No ventilation, No UV	2900	--
No ventilation, UV on	459	84.2
Ventilated at 50-60 lfm, No UV	36	98.8
Ventilated at 100 lfm, No UV	8.4	99.7
Ventilated at 100 lfm, UV on	11.5	99.6
Test 2		
No ventilation, No UV	440	--
No ventilation, UV on	89	79.8
Ventilation at 100 lfm, No UV	9.7	79.8
Test 3		
No ventilation, No UV	5100	--
Ventilation at 50-60 lfm, No UV	27.6	99.5
Ventilation at 100 lfm, No UV	3.5	99.93
Test 4		
No ventilation, No UV	764	--
Ventilation at 50-60 lfm, No UV	5.5	99.3
Ventilation at 100 lfm, No UV	9.7	97.8

a. After Williams and Lidwell.[62]
b. Average number of colonies collected outside the cabinet from 45 cubic feet of air.
c. Removal efficiency compared with no ventilation and no UV.

Williams and Lidwell compared, in a few tests, the aerosol dispersal on the open table with dispersal in a nonventilated open panel cabinet. The results indicated that the nonventilated cabinet offered little protection for personnel. However, when nonventilated cabinets were used with the interior ultraviolet lamps turned on, the number of air-borne organisms escaping from the cabinet was reduced by about 80 per cent (Table XLI). Ultraviolet lamps, however, are seldom turned on when cultures are being manipulated because of the likelihood that the cultures will be inactivated.

In 1959 Couling and Rees at the National Institute for Medical Research in London described a cabinet used to autopsy tuberculous animals in use in that Institute since 1951[66] (Figure 79 on page 220). The exhaust system in this case provides an air velocity through the open panel of not less than 300 linear feet per minute.

In Sweden, Lind has designed several types of ventilated cabinets for use in laboratory operations with tubercle bacilli.[79] A stainless steel cabinet for pre-treatment of gastric washings or urine specimens provides an inlet flow of approximately 110 feet per minute. For sterile operations and for sensitivity tests Lind has devised closed cabinets in which the ventilation system is off during certain operations and then turned on.

The frequency of use of cabinets and other externalization devices in infectious laboratory operations provided evidence of the recognized need for safety equipment. Some type of cabinet was seen in 55 of the 102 laboratories and in each of the 18 countries visited. However, as illustrated in the pictures in this section, it was obvious that recognition of the need for cabinets did little to assure that the devices used provided an adequate amount of protection or that they were properly designed and constructed.

Engineering accomplishments in microbiological cabinet development in the U.S., an effort paralleled by achievements in dry-boxes for radioactive work, have reached a high level. The U.S. Army Chemical Corps, and in particular the Fort Detrick Laboratories, have been leaders in this endeavor. The Canadians, the Swedes, and the British have been active in the development of cabinets for use in their laboratories. To a lesser extent, cabinets of various designs have been developed in Germany, Denmark, and Finland.

One may then reasonably ask, "If over 50 per cent of the laboratories recognized the need for protective cabinets to the extent that some type of cabinet had been purchased or built, why were a great majority of these unsatisfactory?" Certainly in many instances the lack of funds was responsible for the make-shift devices used. In my opinion, however, a factor of equal significance was the lack of understanding by the microbiologists of the criteria for efficient cabinet design. In spite of the fact that the sale of ventilated cabinets is supported by national advertising in leading scientific journals, essential information on the design and use of cabinets has not been communicated to scientists in the infectious disease field.

Among the scientists, agreement was not universal on the need for certain cabinet features, such as the need for ventilation or for filtering the exhaust air. Many laboratory people felt that a nonventilated box offered sufficient protection during manipulations with infectious cultures, a supposition not supported by experimental results. Others saw no reason for filtering exhaust air if it was pumped to the outside. And a number of scientists did not recognize the need for any type of cabinet in infectious laboratory work.

Scientists in the U.S. and Sweden are accepting the ventilated safety cabinet as an essential component of the infectious disease laboratory to a greater degree than in other countries. Larger universities, hospitals,

research institutes, and drug firms are utilizing cabinets and cabinet systems, particularly in equipping newly constructed laboratories. The factor of cost in the purchase of cabinets cannot be ignored. Except for the utilization of temporary plastic enclosures, at present U.S. prices, the laboratory director must spend from $1000 to $3000 to buy and install a ventilated cabinet which will provide 15 to 20 square feet of protected working surface. More complex cabinet systems may cost as much as $500 per linear foot. Clearly the need exists for the development of lower-priced cabinets without sacrificing functional efficiency.

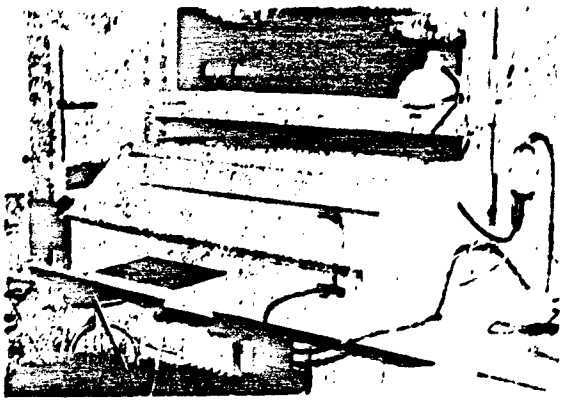
Figures 82 through 91 show a number of the safety cabinets in use in the laboratories in various countries. The photographs are grouped to illustrate objectionable or desirable features.

Figures 82 and 83 show examples of nonventilated cabinets used in infectious disease laboratories. Similar cabinets, sometimes called "quiet hoods," were used frequently in noninfectious tissue culture operations. Most of the nonventilated cabinets used with pathogens contained germicidal ultraviolet lamps. Wood was the most common construction material and as often as not the interior surfaces were not painted or coated. The cabinet in Figure 82, A has two slide-out compartments below the table top; one a board for note taking and the other a rack which holds a pipette discard container. 82, B is a cabinet formerly used for laboratory manipulations of cultures of Pasteurella pestis. C is a cabinet presently used for work with Coccidioides immitis. The remaining photographs in Figures 82 and 83 show other characteristics of nonventilated cabinets. Obviously most of these cabinets were "homemade."

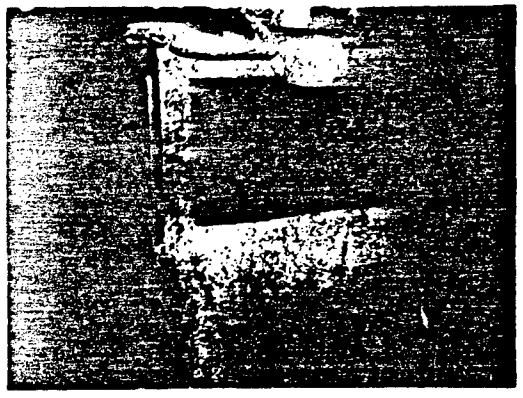
Cabinets shown in Figure 84 are typical of those which do not have exhaust blowers or filters but are vented directly to the room. In two instances, 84, A and B, it was felt that the heat from Bunsen burners in the cabinets would inactivate air-borne pathogens escaping through the vent. 84, C shows a vented, wooden cabinet for virus work which is lined with "Formica" and utilizes a sliding storm window for the front panel. A window shade is provided and is pulled down when the ultraviolet lamps are turned on. 84, D is a cabinet used to seal vials of lyophilized cultures and solutions of various live antigens. The original function of the empty chamber on top of the cabinet was uncertain. A plenum for ultraviolet lamps was provided on the cabinet in 84, E. However, the lamps were no longer used and this cabinet, like the others, vented directly to the room. 84, F shows a vented cabinet used for injecting animals.

Figure 85 shows a group of cabinets which lacked exhaust blowers and filters but which were vented to the outside of the laboratory buildings. This practice is undesirable because outside winds and pressure differentials could create a reverse flow of air from the cabinet.

Cabinets with exhaust blowers which discharged the air to the outside but which lacked bacterial filters are shown in Figure 86. An insufficient amount of air was withdrawn from most cabinets of this type.



A



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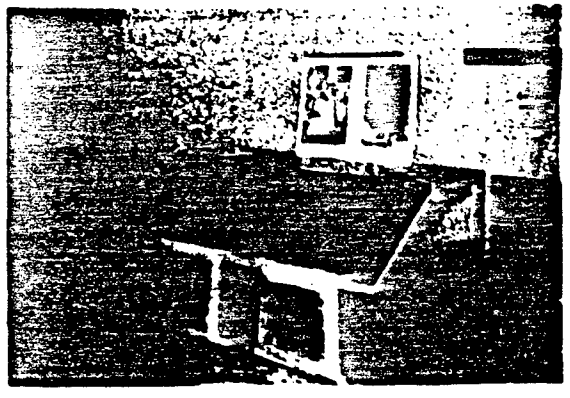
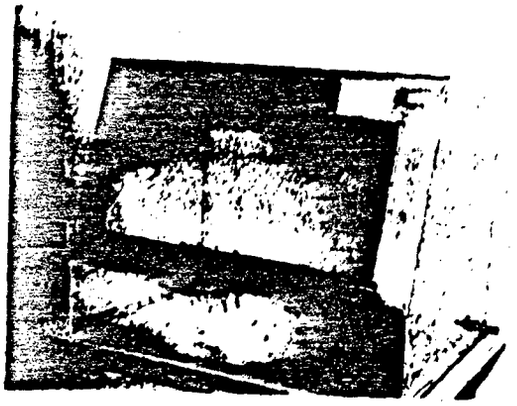
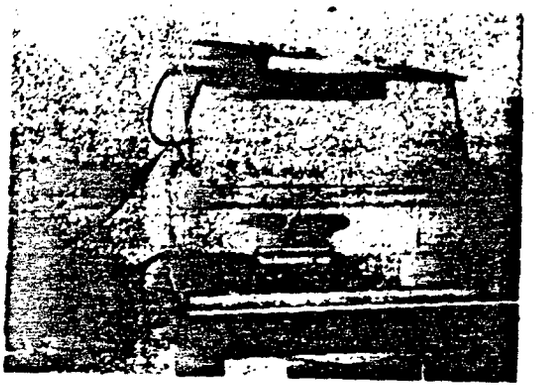


C

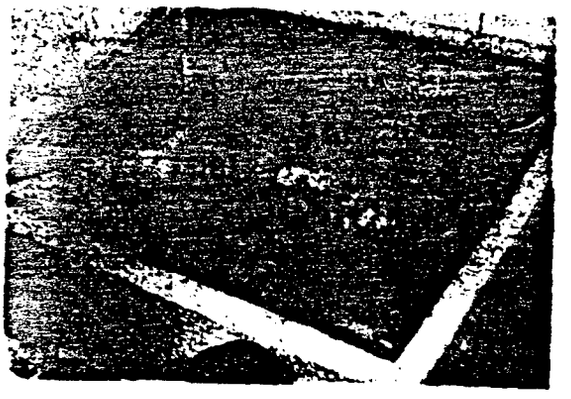
Figure 82. Nonventilated Cabinets.
A. Wood Cabinet for TB Work.
B. Wood Cabinet for P. pestis Work.
C. Wood Cabinet for C. immitis Work.



D



E



F

D. Aluminum Cabinet.
E. Plexiglas Cabinet for Weighing.
F. Closed Wooden Cabinet for TB Work.

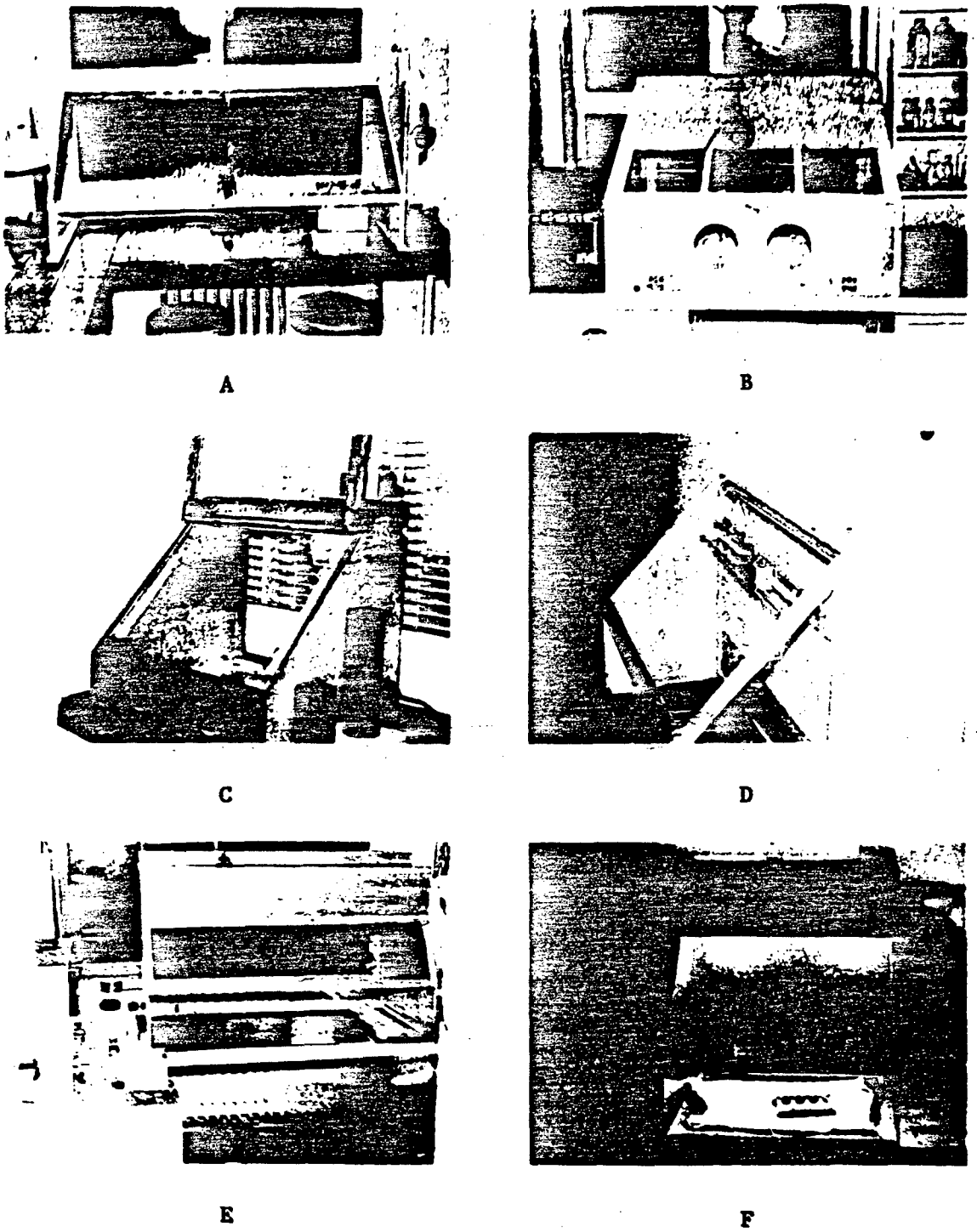


Figure 83. Nonventilated Cabinets.
A, B, C, and D. Cabinets with Glass Backs for Virus Work.
E. Cabinet with Glass Back for TB Work.
F. Metal Cabinet for TB Work.

The cabinets shown in Figure 87 illustrate a number of undesirable features. An "inoculating hood" shown in 87, A has no exhaust blower, but air exiting through the inverted funnels (under which are placed the gas burners) passes over a small strip-bar electric heater on the top of the hood. It is doubtful that the temperature of this unit is sufficient to produce sterility of the air passing over it. The air exhausts directly to the room. The "pathological cabinet" shown in 87, B is made by John Bass, Ltd., Crawley, Sussex, England. A self-contained blower exhausts air through a dust filter and directly to the room or through a duct to the outside. Although the tray holding the filter pad may be removed without touching the filter material, the efficiency of the filter is low. This cabinet measures 36 inches wide, 25 inches deep, and 33 inches high. The cabinet shown in 87, C was developed for operations with tubercle bacilli.[62] It has an adequate exhaust velocity, but the low-resistance paper filter is no more than 60 to 70 per cent efficient in removing small air-borne particulates. The virus cabinet in 87, D has an inadequate amount of exhaust air. A battery of ultraviolet lamps in the exhaust duct is provided to decontaminate the air. 87, E and F are examples of cabinets provided with very small exhaust lines and "in line" cotton filters. The amount of air exhausted is inadequate.

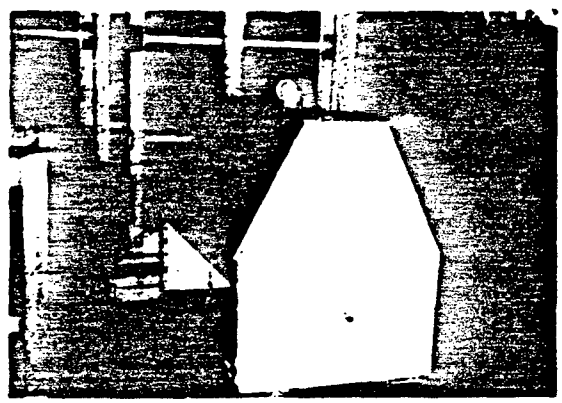
Figure 88 illustrates still other difficulties in cabinet design; one being that cabinets may be too small for the laboratory operations to be done in them. For example, although the cabinet being installed in 88, A will have an efficient air exhaust and sterilizing system, the small height of the cabinet prohibits the use of pipettes and other laboratory apparatus. Likewise, the size of the aluminum cabinet shown in 88, B is such that the tray for discard pipettes and other apparatus must be placed outside of the cabinet. The cabinet shown in 88, C and D has two undesirable features: a sliding front and a damper by which the amount of exhaust air can be regulated. Technicians sometimes used these cabinets with the dampers closed or with the sliding doors fully opened.

The cabinets shown in Figure 89 utilize natural gas burners in the exhaust ducts. The burners create an inward flow of air into the cabinet and heat the exhaust air to a sterilizing temperature. While the use of gas in this manner may create an undesirable explosion or fire hazard, the cabinets in general are efficient if the openings into the cabinet are restricted.

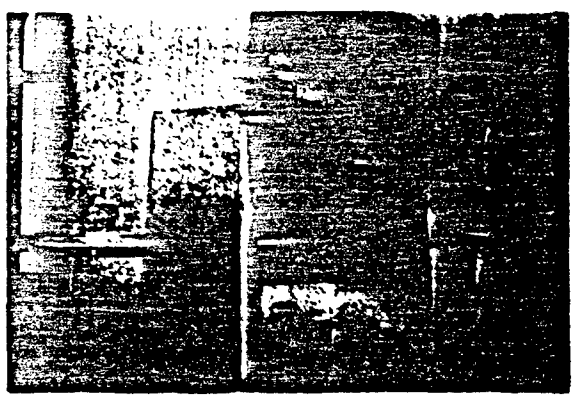
Figures 90 and 91 show cabinets in the U.S., Canada, England, and Sweden which were judged to meet most of the criteria given on page 223.

Cabinets of a design developed by the U.S. Army Biological Laboratories were found in several laboratories (90, A). This cabinet as well as those in B and C are commercially available in the U.S. and are the best cabinets seen during the study fellowship. The ventilated cabinet shown in picture D was designed by personnel at the Central Public Health Laboratories in Toronto. The exhaust filter is of spun glass mats. Operations are normally carried out with an open front panel, The solid panel shown in the photograph is used only during cabinet decontamination. Several different cabinet shapes have been developed, some with sliding viewing panels. These cabinets are fabricated by S. H. Newman Co., Ltd., Toronto.

A



B

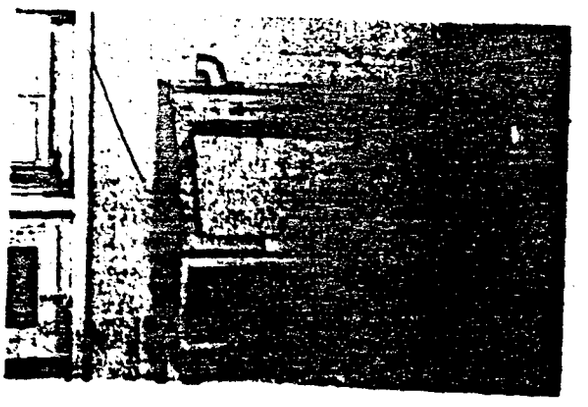


C

Figure 84. Cabinets Vented to the Room.
A. Double-Sided Glass Cabinet.
B. Double-Sided Metal Cabinet.
C. Formica Lined Wooden Cabinet with Sliding Front.

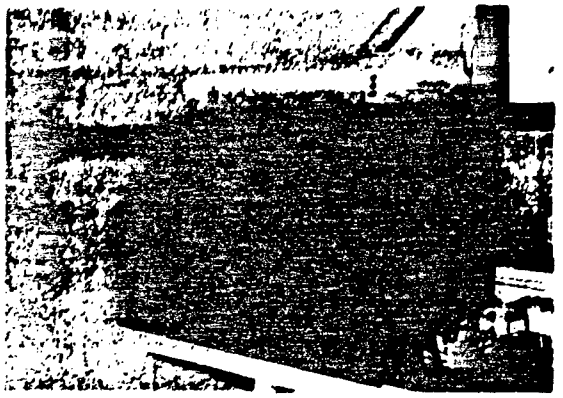
D

E

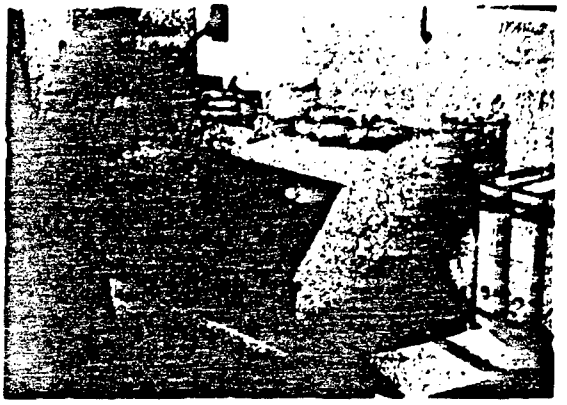


F

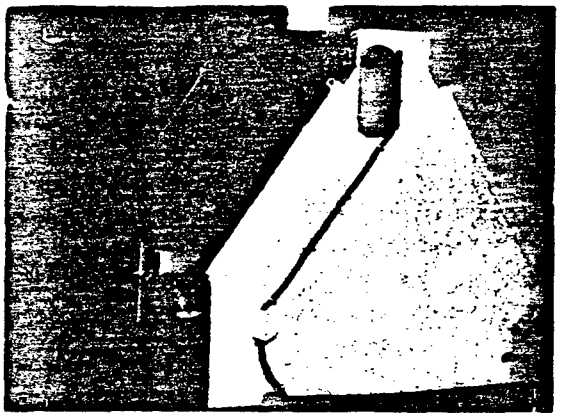
D. Metal Cabinet.
E. Wooden Virus Cabinet.
F. Animal Inoculation Cabinet.



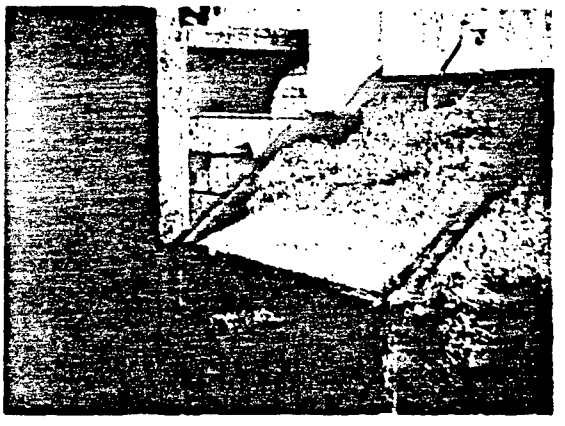
A



B

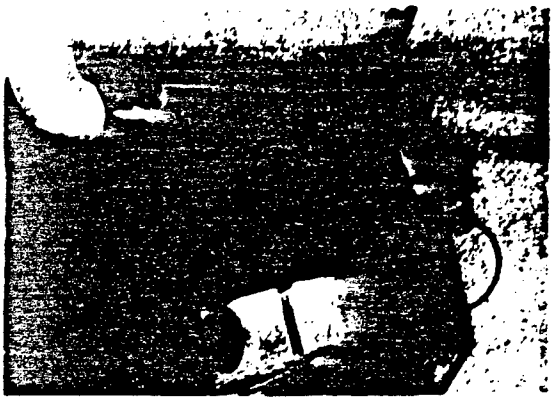


C

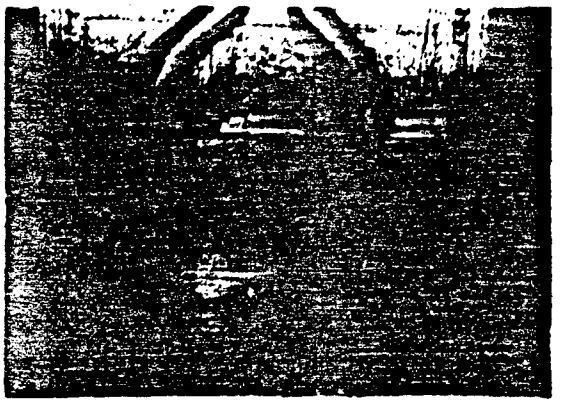


D

Figure 85. Cabinets Vented to the Outside.
A. Stainless Steel Cabinet for TB Work.
B. Metal Cabinet for Virus Work.
C. Double-Sided Wooden Cabinet for TB Work.
D. Glass Cabinet for TB Work.

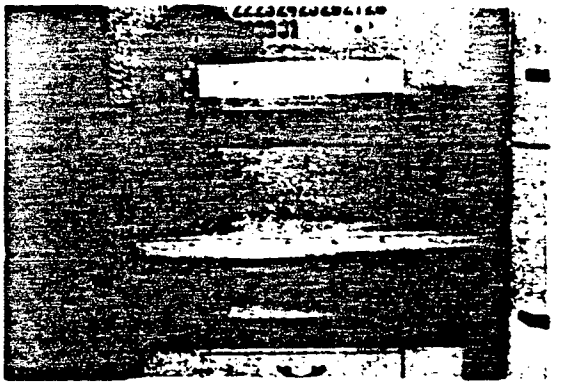


A



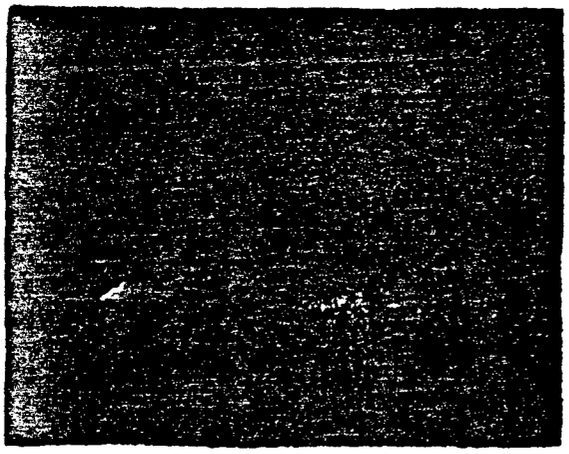
B

C

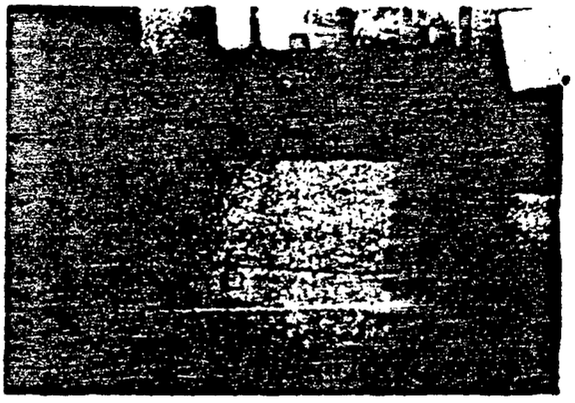


D

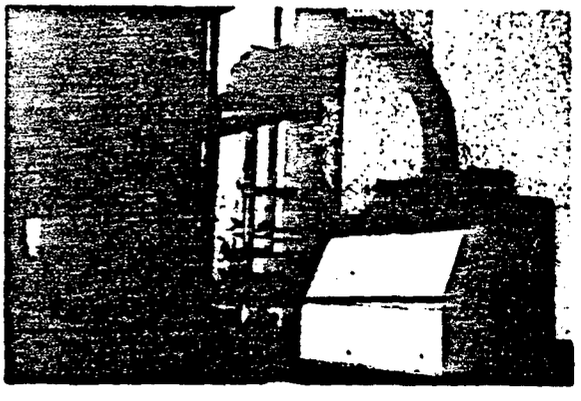
Figure 86. Ventilated Cabinets Without Air Exhaust Filters.
A. Double-Sided Closed Cabinet for TB Work.
B. Two-Person Cabinet with Glass Back.
C. Cabinet with Sliding Front for TB Work.
D. Aluminum Cabinet for Virus Work.



A

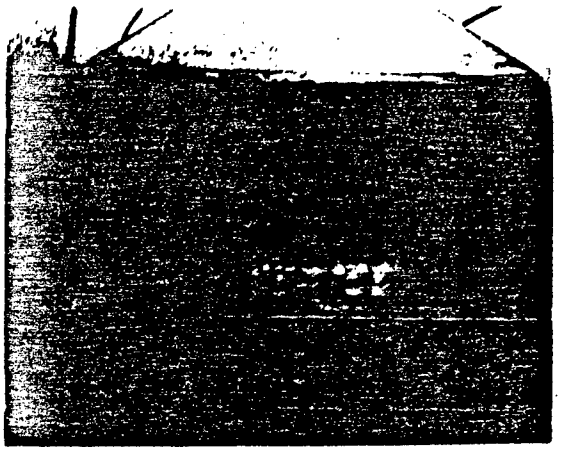


B

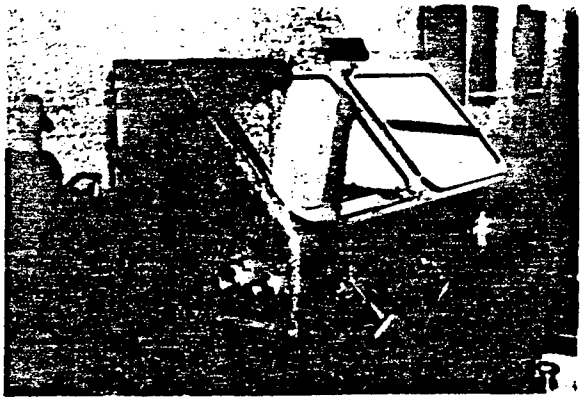


C

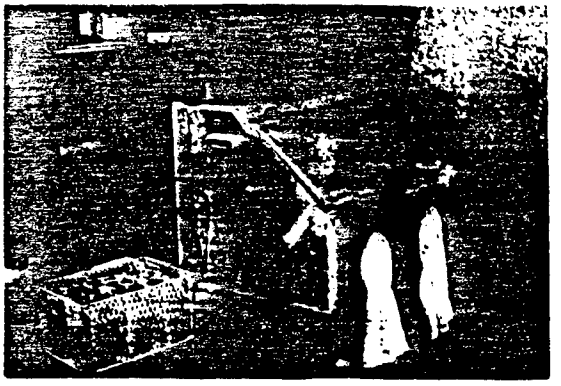
Figure 87. Miscellaneous Cabinets.
A. Vented Inoculating Hood.
B. Pathological Cabinet.
C. Ventilated Cabinet for TB Work.



D

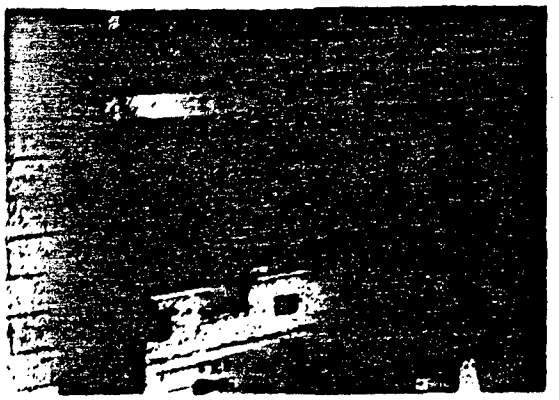


E

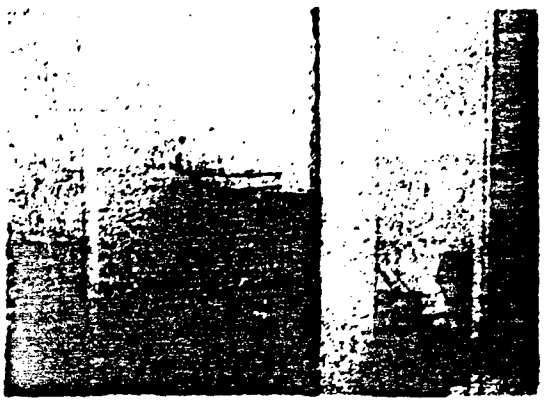


F

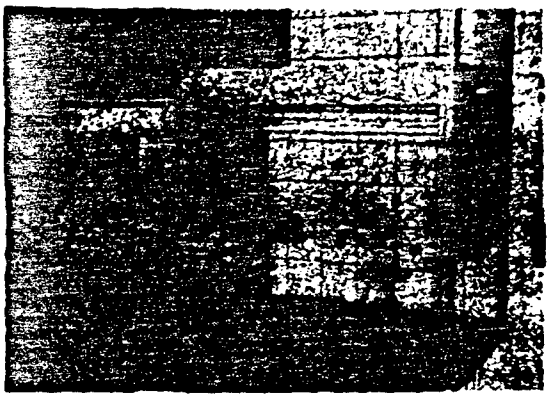
D. Ventilated Cabinet for Virus Work.
E and F. Ventilated Cabinet with Small Exhaust.



A



B

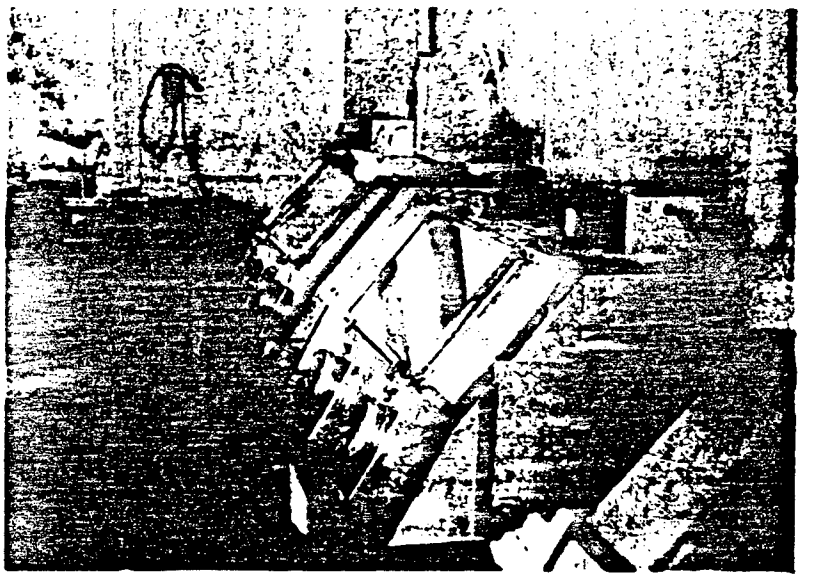


C

D

Figure 88. Miscellaneous Ventilated Cabinets.
A. Small Stainless Steel Cabinet.
B. Small Aluminum Cabinet.
C and D. Glass Cabinet with Sliding Front.

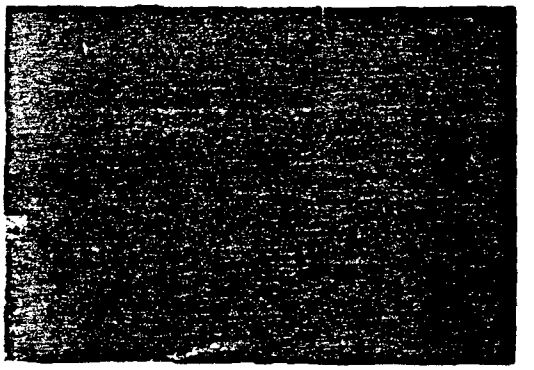
A



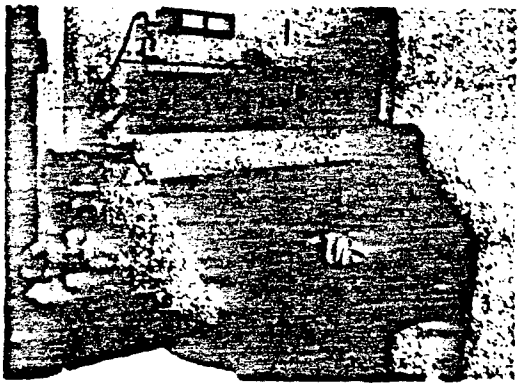
B

Figure 89. Cabinets with Gas-Burner Exhaust Systems.
A. Typhus Vaccine Production Cabinet.
B. Cabinets for Virus Work.

A

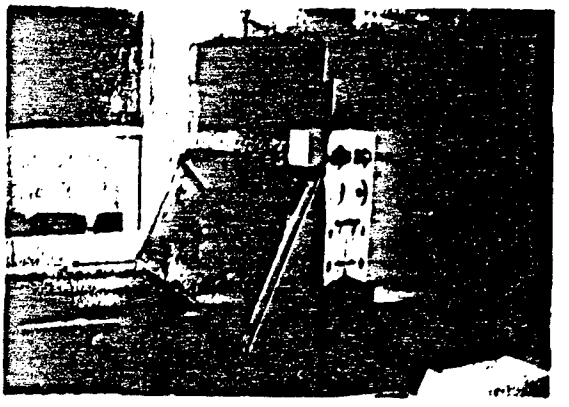


B



C

Figure 90. U.S., Canadian, and British Ventilated Cabinets.
A. Cabinet Designed by the Biological Laboratories.
B and C. Commercially Available U.S. Cabinets.



D

E

D. Commercially Available Canadian Cabinet.
E. British Portable, Aluminum Cabinet.

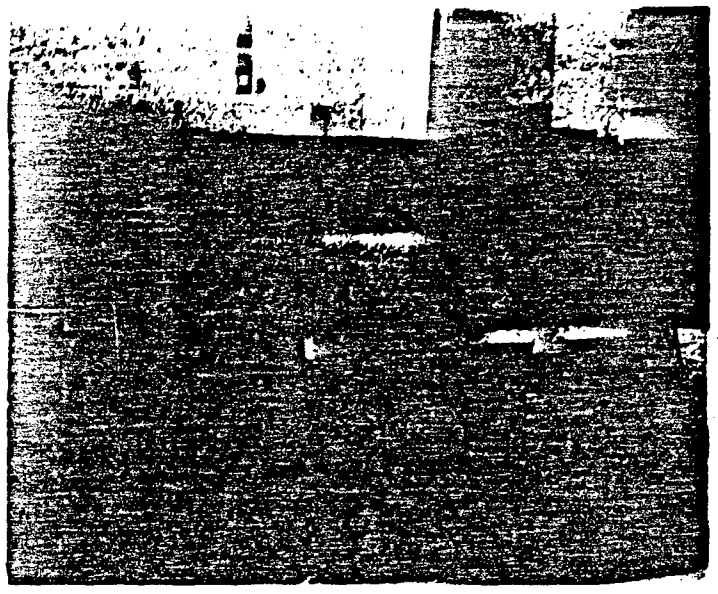
Figure 90, E shows an all aluminum, portable ventilated cabinet with filter and exhaust blower which was developed at the Microbiological Research Establishment in Porton, England, by Dr. H. M. Darlow. Being 45 inches wide and 28 inches deep, and estimated to cost only about $336.00 (without filter), this is one of the best portable type cabinets I have seen. A high efficiency (99.95 per cent) cotton-asbestos filter is located in the exhaust duct between the cabinet and an Axilvane exhaust blower. Exhaust air is discharged directly to the room. A draft gauge above the filter indicates when the filter resistance has increased enough to require its replacement. The filter-blower assembly may be easily detached and a new assembly bolted in place. To facilitate cabinet sterilization a small funnel on top of the cabinet is used for introducing formaldehyde solution into a small electrically heated cup inside the cabinet. When contaminated filter units are removed they are sterilized by autoclaving. Fluorescent and ultraviolet lamps (in water-proof rubber sockets) are located inside the cabinet and connected to outside control switches. As shown, the cabinet may be used with or without attached rubber gloves. The six-inch diameter opening, natural rubber gloves are made by Veedip, Ltd., St. Helens Works, Slough, Bucks, England. The slanted front of the cabinet is hinged and the safety glass is held in place with an H-type gasket.

The cabinets shown in Figure 91 were seen in Swedish laboratories. Although a number of well-designed cabinets were seen in this country, the best were those designed by Dr. Arne Lind in Gothenburg.[79] One of several stainless steel prototype models which have been developed for the new buildings presently under construction is shown in 91, C. It is provided with absolute filters which are changed from the inside of the cabinet. An exhaust blower provides an inward air flow of 100 to 110 feet per minute. It is estimated that these cabinets will cost approximately $2500 each (12,500 Swedish kroner). Sixty-three cabinets are to be installed in the new Gothenburg laboratories.

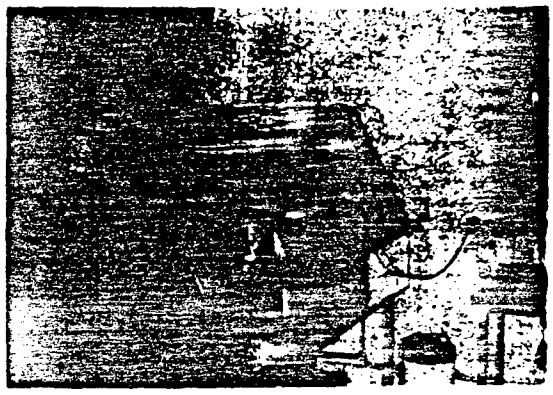
F. ULTRAVIOLET

Applications of germicidal ultraviolet radiation in microbiological laboratories have been adequately studied by investigators at the Biological Laboratories.[80-84] Not only have the ways in which ultraviolet lamps may be used to reduce and control infectious hazards been investigated, but design and maintenance requirements have been formulated and information gathered on the limitations applicable to the use of the germicidal radiation. Based on these studies, an attempt was made to judge the effectiveness of use of ultraviolet at each institute visited. In general, the criteria used for this evaluation were as follows:

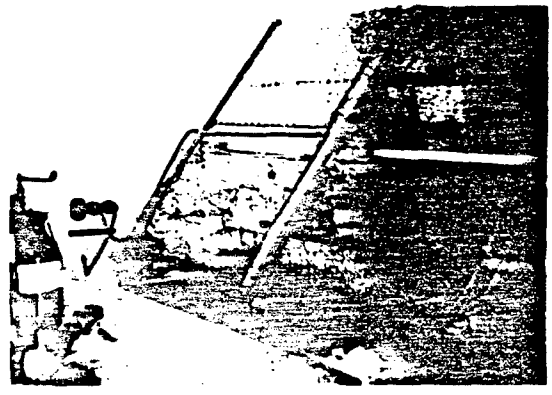
1. Were the lamps used?
2. Were the lamps cleaned at appropriate intervals?
3. Were the lamps tested and changed regularly?
4. Were an adequate number of lamps used?
5. Had the installation been safety tested to see if it performed in the expected manner?



A



B



C

Figure 91. Swedish Ventilated Cabinets.
A and B. Stainless Steel Cabinets in Stockholm.
C. Prototype Stainless Steel Cabinet in Gothenburg.

Low-pressure, mercury-arc lamps producing ultraviolet radiation in the region of 2537A were used in laboratories in every country and in 73 per cent of the laboratories visited. Ultraviolet was one of the most universally used safety devices. The following list illustrates the variety of applications for which ultraviolet was employed:

1. In safety cabinets and hoods
2. Irradiation of the upper air
3. Direct irradiation in laboratories
4. Personnel air locks
5. Equipment air locks and pass boxes
6. Irradiation of isolation cubicles
7. Centrifuge enclosures
8. Treatment of supply and exhaust air from rooms and buildings
9. Treatment of exhaust air from safety cabinets
10. Room air conditioners
11. Portable apparatus for emergency decontamination
12. Petri plate pouring rooms
13. Room air recirculating apparatus
14. Decontamination of the surfaces of bacterial filters

Only about one fourth of the laboratories using germicidal lamps were employing them at maximum efficiency. A number of ultraviolet installations had been turned off and were no longer used. The most frequent error was that the germicidal lamps were not cleaned or changed at appropriate intervals. It was not uncommon to be shown ultraviolet lamps that had not been cleaned or changed in two or three years. In relation to personnel safety, the inefficient use of ultraviolet radiations is a serious problem because it creates a false sense of security. It was clear that in most laboratories the difficulties stemmed from a lack of available information about methods of use of ultraviolet and a lack of general understanding of its limitations. In general, ultraviolet installations in the U.S., Sweden, and England were superior to those in other countries.

Although cold cathode type lamps are available both in the U.S. and in Europe, hot cathode lamps are used most frequently. Since hot cathode lamps have their maximum output at a bulb wall temperature which is obtained in relatively still air, subjecting them to strong air currents cools the bulb and lowers the output. This mistake was made in a number of laboratories.

Although ultraviolet can be used effectively to obtain a 90 to 95 per cent reduction of air-borne organisms in moving air supplies, higher efficiencies are difficult to obtain because of the large number of lamps required. In the 21 air systems in which ultraviolet was used to treat incoming (13 instances) or outgoing (8 instances) air, no more than ten had been tested to determine the effectiveness of treatment.

Another factor which became apparent during discussions with scientists in various laboratories was that ineffective ultraviolet installations were, in part, a result of exaggerated claims made by sales representatives. Understandably, as a result of this, a number of scientists were opposed to its use in the laboratory or regarded its use merely as a window dressing.

In Sweden several scientists were well informed about the use of ultraviolet. Among these were Professor Hans E. Ronge, Professor of Hygiene at Lund University and Professor Gunnar Laurell, Institute of Bacteriology, at the University of Uppsala.[85]

In England, an ultraviolet "air washer" has been recently designed and tested by scientists at the Microbiological Research Establishment. This apparatus utilized a four-foot section of aluminum tubing about 12 inches in diameter (Figure 92). Suspended in the tube were four 30-watt, hot cathode ultraviolet lamps. A fan at one end draws about 1000 cubic feet of air per minute through the tube. The air is irradiated for about 0.2 of a second. At maximum output the lamps produce a total of about 32 watts of germicidal radiation. This exposure-concentration ratio is adequate to inactivate most air-borne microorganisms. Tests with Serratia marcescens showed that the air washer had the same removal effect on the air-borne microorganisms as ventilating an averaged size room at a rate of 20 changes of air per hour. Since control tests showed S. marcescens to have a natural decay rate with the ultraviolet off equal to seven changes of air per hour, the final efficiency, with vegetative organisms, is roughly equivalent to 27 changes of air per hour. The air washer is portable and can be easily moved into a room following an accidental spill of infectious material.

At the Colindale installation of the Central Public Health Laboratories in London, a somewhat similar ultraviolet air washer had been tested. The apparatus was shown to be 100 per cent effective when used in the laboratory with artificially produced aerosols, but when placed in hospital ward rooms there was little difference in the average over-all air counts.

Ultraviolet lamps were frequently used inside cabinets: 73 per cent of the ventilated cabinets and 92 per cent of the nonventilated cabinets examined had ultraviolet lamps inside.

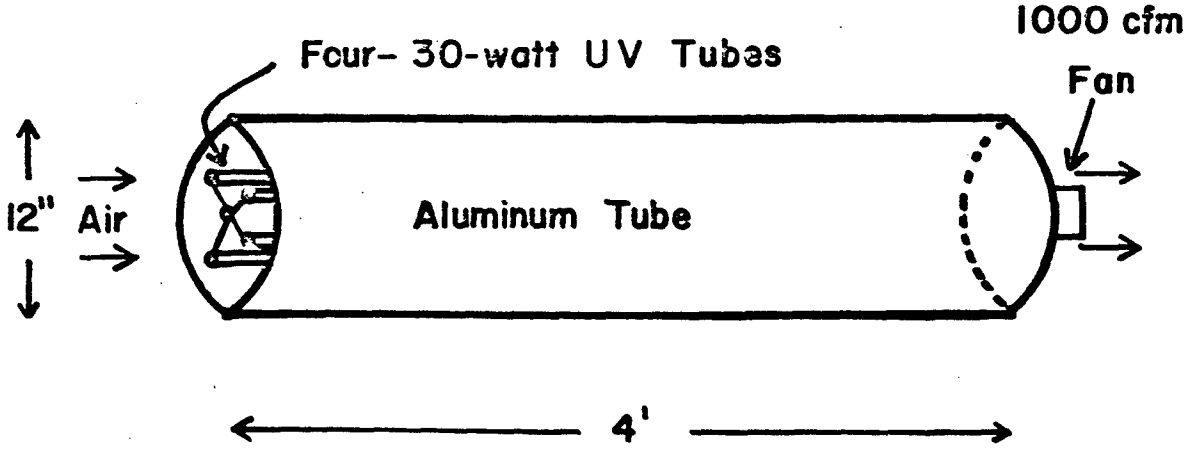
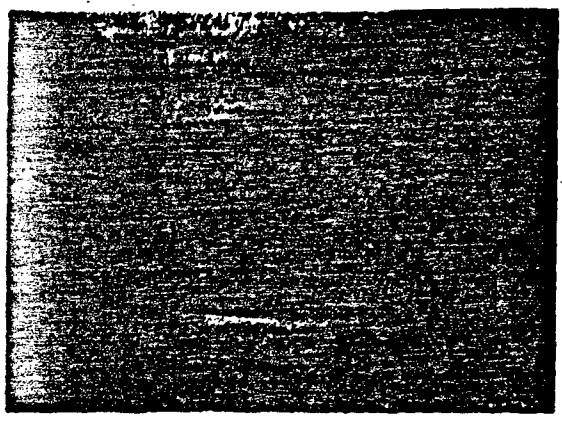
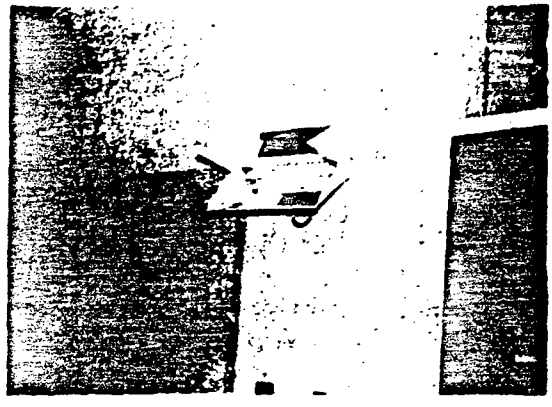


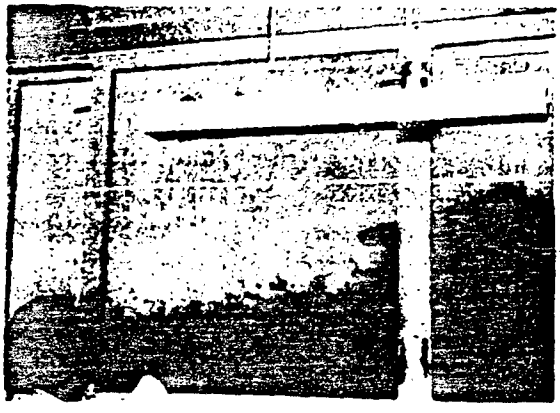
Figure 92. Ultraviolet Air Washer.



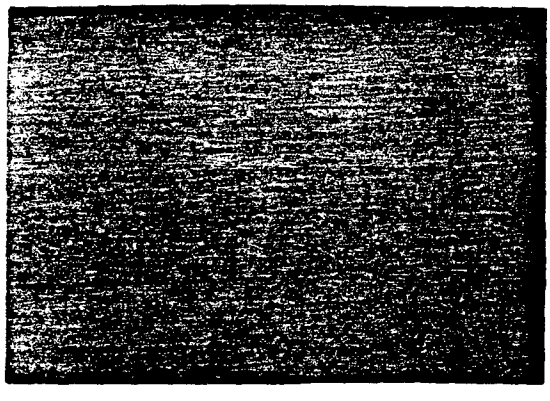
A



B

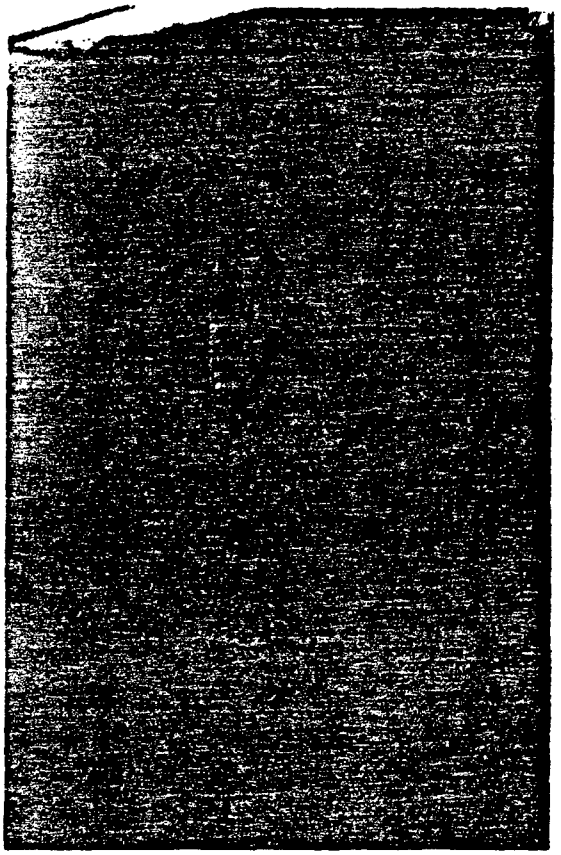


C

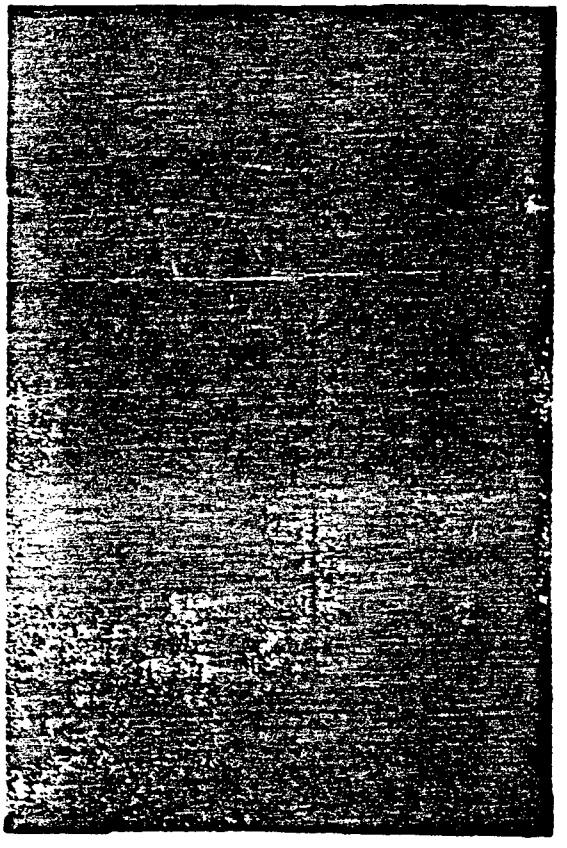


D

Figure 93. Ultraviolet Installations.
A. Upper Air UV Fixture.
B. Opening Type UV Wall Fixture.
C and D. Reversible UV Fixtures.

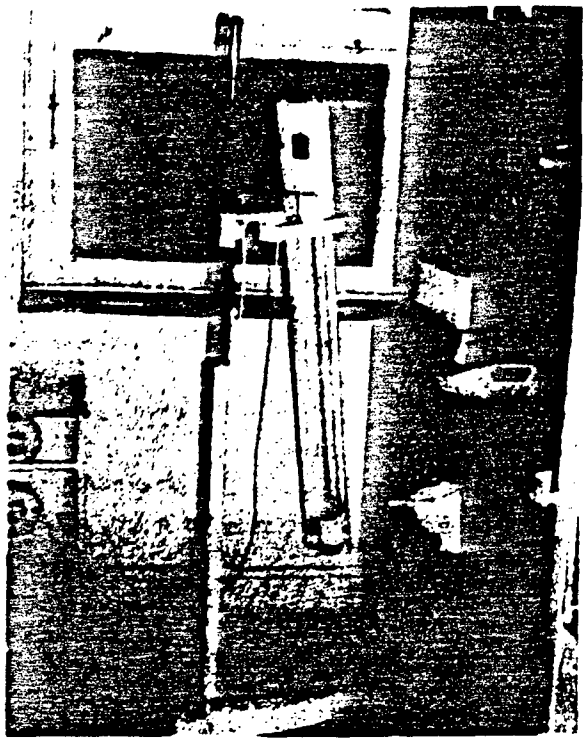


E

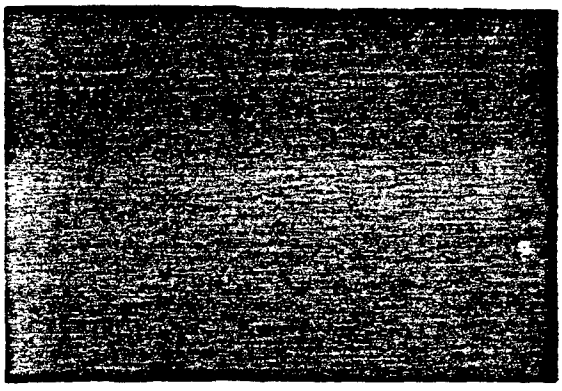


F

E. Five-Fixture Door Barrier.
F. One-Fixture Door Barrier.



A



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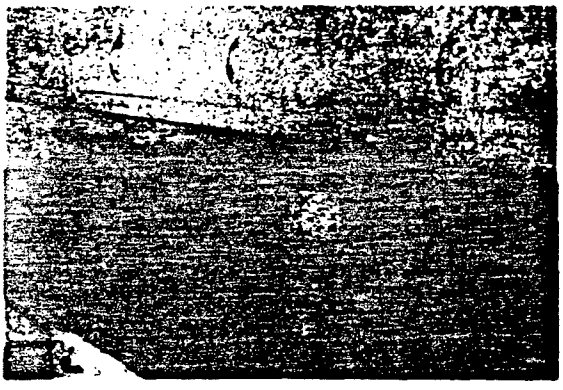
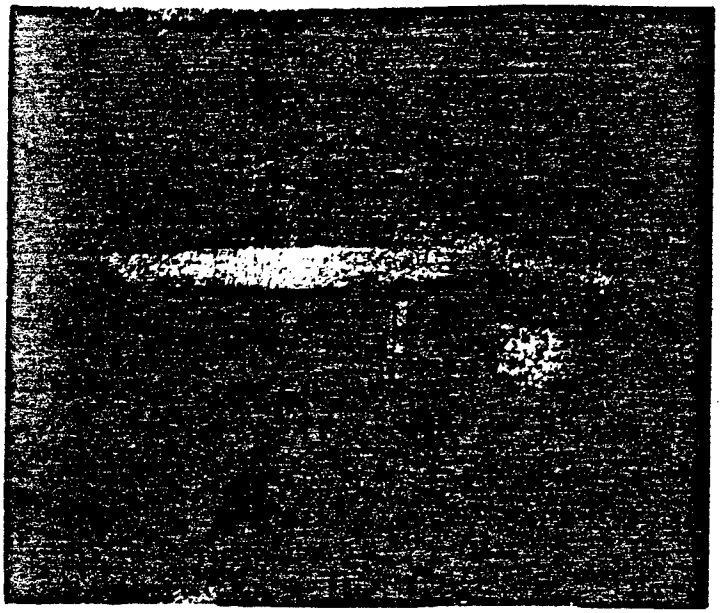
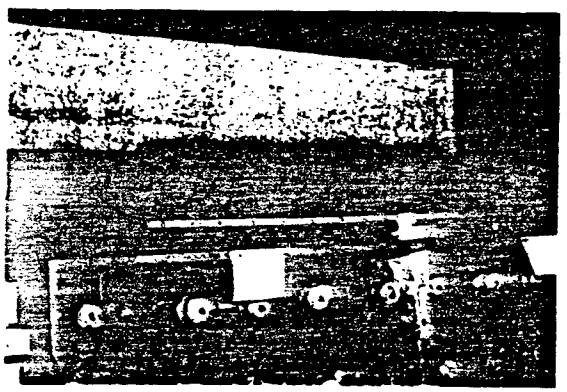


C

Figure 94. Miscellaneous Ultraviolet Applications.
A and B. Portable UV Fixtures.
C. UV Over Media Pouring Table.



D



E

F

D. UV Over Centrifuges.
E. UV Fixture in an Incubator.
F. UV Fixtures in an Animal Room.

Figure 93 shows examples of irradiation devices in laboratory rooms and change rooms. In 32-laboratory buildings upper air irradiation devices such as shown in 93, A were used. A few of these were wall fixtures which opened to allow the radiation to be directed downward when desired, as shown in 93, B.

Reversible ultraviolet fixtures as shown in 93, C and D were used in seven laboratories in Sweden and Denmark. These were generally pointed to irradiate toward the ceiling in the daytime and toward the floor at night. Ultraviolet door barriers were found at 17 of the institutions visited. The best type was that shown in 93, E, but in most instances the barrier consisted of a single fixture hung over the door as shown in 93, F. Air locks with ultraviolet lamps were seen in 27 of the 102 laboratories. These were mostly for equipment rather than for use by laboratory personnel.

Figure 94 shows other typical applications of germicidal ultraviolet radiation. In 12 European laboratories portable ultraviolet lamps were on hand to be used for emergency decontamination. These were mounted on stands that could be conveniently rolled from room to room (94, A and B). In 27 laboratories ultraviolet lamps were used to provide direct irradiation of room surfaces. Frequently lamps were placed directly over benches or tables used to prepare agar plates, as illustrated in 94, C. In one tuberculosis laboratory, swinging ultraviolet fixtures, as shown in 94, D, were used to irradiate the inside of centrifuges when they were opened. Ultraviolet fixtures were occasionally seen in incubator and animal rooms, as shown in 94, E and F.

VIII. MISCELLANEOUS FELLOWSHIP ACTIVITIES

A. EXCHANGE OF SAFETY INFORMATION

One of the deterrents to better safety technology in microbiological laboratories is the lack of communications. During the fellowship many scientists referred to articles published by the U.S. Army Biological Laboratories. Yet, communications have not been sufficient to provide a full understanding of the Chemical Corps' advances in the field of microbiological safety. This was particularly true for (a) design of infectious disease laboratories, (b) design and use of ventilated cabinets, (c) use of ethylene oxide as a gaseous sterilant, and (d) use of germicidal ultraviolet radiation. In 63 per cent of the laboratories the director or the staff requested help on specific laboratory safety problems (Table XLII).

TABLE XLII. RELATIVE FREQUENCY OF REQUESTS FOR LABORATORY SAFETY INFORMATION

SUBJECT	RELATIVE FREQUENCY
Safety equipment and apparatus	59
Regulatory information	44
Laboratory procedures	40
Training and training films	31
Laboratory design criteria	19
B-virus infections	2

Over one half (69 per cent) of the laboratory chiefs expressed the opinion that some type of monograph on microbiological safety should be published. Many scientists frankly admitted that they were unable to spend the time that would be necessary to consult the various technical journals for published information on this subject.

B. HOSPITAL INSPECTIONS

During the research study I inspected 11 hospitals in seven countries. While a study of hospital contagion problems was not a specific objective of the fellowship program, many of the control and isolation procedures recommended for infectious disease laboratories apply equally as well in hospitals. Also, hospitals have an obligation to insure that infectious microorganisms used in their laboratories are not allowed to escape to other parts of the hospital.

Because of the limited number of hospitals inspected, no over-all conclusions can be drawn. It is significant that some of the laboratories visited were carrying on projects for improving hospital contagion problems, particularly the problem of the spread of staphylococcal infections among patients and hospital personnel. The hospital infection problem is primarily one of environmental control and containment. It would seem to be a reasonable assumption that microbiologists who have been successful in solving laboratory containment problems in these areas would be in a good position to advise hospital authorities on environmental control and containment measures.

In laboratories doing hospital cross-infection studies there was a frequent need for devices to sample microorganisms in the air. Laboratories in England were generally well acquainted with air sampling devices, but they were seldom seen in the U.S. and in other countries.

In the following paragraphs some details of inspections at three hospitals are recorded to illustrate these activities.

1. An Australian Hospital

This 215-bed chest hospital was completed and occupied in August 1958. It is used primarily for tuberculosis patients. The five-story building is of modern design with picture windows, balconies for each room, and a penthouse in which are located equipment rooms and rooms for infected laboratory animals. The inspection results and recommendations were as follows:

a. Laundry Handling

On each floor, discard laundry was divided into three portions. Laundry contaminated with feces and urine was placed by the nurse on each floor into a special boiling pot, boiled for a short period and then carried by hand to the laundry room in the basement. Clothing and linen soiled with pus and blood was placed in plastic bags and carried to the laundry room. Regular linen was sent to the basement room via a laundry chute.

Study of the laundry boiling procedure showed it to be unsatisfactory from several points of view. When the work shift reported for duty, it was not always clear whether the contaminated laundry had or had not been boiled by the previous shift. During the sorting and boiling process ample opportunity existed for the nurses to contaminate their hair, skin, shoes, and clothing. The same nurses served the patients' rooms on that floor. In addition the dirty linen rooms were at a positive pressure in relation to the corridor, and the room doors were customarily left open. The laundry chute itself was under a negative pressure.

In the basement the chute terminated in a large empty room used for sorting the laundry. All linens and laundry brought to the basement and laundry arriving via the chute were spread out on the floor, sorted, counted, and loaded into carts for delivery to an outside laundry. This procedure was highly undesirable, since two of the three types of laundry were still contaminated at this point. Once each day the floor of the room was washed, but the room was obviously potentially contaminated most of the time. In addition, it was found that the sorting room was under a positive pressure and discharged air into the basement corridors and from there to the rest of the hospital through the open stairwells. The following recommendations were made:

(1) Install autoclaves in the sorting room and sort only laundry which had been sterilized.

(2) Deliver all laundry to the basement in plastic bags.

(3) Install an air exhaust system with bacterial filters in the laundry room and maintain the room at a negative pressure relative to the basement corridor.

b. Solid Waste Incinerator

Each floor of the hospital had a chute leading to a coal-fired incinerator in the basement. The incinerator also served as the heating furnace and steam generator. Since the incinerator was operated only during certain hours of the day there was no control of direction of air movement in the chute and little assurance that the inside of the duct work would not become contaminated. It was recommended that the use of the incinerator chutes be discontinued and that contaminated combustibles be delivered to the basement in closed containers or plastic bags.

c. Hospital Air System

The hospital had a recirculating air system with no filters and no means of controlling direction of air flow. Installation of air filters and regulation of air pressures were recommended. The operating rooms had a separate air system and were maintained at a positive pressure in relation to the rest of the hospital, but the air was recirculated without filtration.

2. A Greek Hospital

This Athenian hospital of 200-bed capacity was used primarily for patients with tuberculosis. Construction of the hospital was finished in 1955. The director requested that I inspect the operating room procedures and equipment and suggest improvements. The staff were concerned about post-operative infections.

The two operating rooms and the preparation and sterilizing rooms all opened on a corridor at the end of one wing. Contaminated materials were removed through the clean area. It was found that closing off one door and installing a suitable ultraviolet air lock permitted a logical flow of materials without the necessity of taking contaminated materials through clean areas.

Ventilation in the main operating room was provided by a window air conditioning unit installed in such a manner that cool air was blown toward the floor. The air currents at the floor level were obviously strong enough to raise an aerosol of dust. It was recommended that the air be deflected from the floor and that ultraviolet lamps be placed in the air conditioning unit.[80]

Although a small autoclave was provided in the instrument sterilizing area, the chief nurse insisted that instruments should be boiled to achieve sterility rather than by autoclaving ("I've done it this way for 20 years."). Even if boiling produced sterility there appeared to be little chance that the instruments would remain sterile during subsequent handling. It was the surgeons' desire that the instruments be autoclaved, but the nurse had consistently refused. This, of course, was a management problem.

Foam rubber neck, back, and arm rests were frequently used on the two operating tables. In spite of the fact that rubber sheets were placed over these rests they frequently became contaminated with blood and other exudates. The rests could not be autoclaved because they would become hard. The director wished to know if ethylene oxide sterilization was feasible. After examining the foam rubber rests, it appeared more feasible to try to secure rests that could be autoclaved. The presence of dried blood and pus would make gaseous sterilization very difficult.

3. A U.S. Hospital

The new operating suite of a 650-bed hospital was inspected. There were 13 operating rooms with the requisite number of clean-up, sterilizing, and recovery rooms. The entire suite was designed for environmental control during operating procedures. Essential features provided were (a) filtration and ultraviolet irradiation of room air supply, (b) balance of air pressures within rooms, (c) physical separation of sterile and potentially contaminated areas, (d) through-the-wall autoclaves, and (e) germicidal ultraviolet irradiation of operating and examining rooms.

These facilities, combined with rigid regulations, resulted in almost no unexplained post-operative infections. Although the cost of this facility was high, it demonstrates that the containment principles in infectious disease laboratories have much in common with those desirable in hospital operating rooms.

C. ILLUSTRATED LECTURES

During the fellowship 46 illustrated lectures were presented at 43 laboratories in 17 countries. Personnel at 23 additional laboratories visited were invited to lectures which were given at one of the 43 laboratories. Thus, personnel from 65 per cent of laboratories visited attended the lectures. The subject matter of the lecture material was varied to meet local needs. To illustrate, in countries where many laboratories often do not have funds to purchase animals for experimental use, it would have been improper to lecture on the need for expensive microbiological cabinet systems. The Appendix lists the places where lectures were presented.

It is estimated that the total audience reached through these presentations exceeded 3000 persons. At 12 lectures only professional personnel attended. In the remainder, professional persons, students, and technicians attended. A few laboratory directors allowed laboratory workers and animal caretakers to attend. All lectures were presented in English. In only two laboratories was it necessary to lecture through an interpreter.

An effort was made to evaluate the general reception of the information presented. After 42 of the 46 lectures the chairman asked for questions from the floor. Questions were asked following 37 lectures. In only one instance were questions asked regarding biological warfare. In this case the university professor had previously asked his medical students to prepare a theme on the potentialities of biological warfare. The questions most frequently asked concerned the laboratory use of ultraviolet radiation and ethylene oxide gas. Next in frequency were questions on safety equipment or devices and techniques to prevent laboratory infections.

D. LOANS OF AIR SAMPLING DEVICES

To anyone seriously concerned with assessing the safety of procedures and equipment in the infectious disease laboratory, the use of an adequate air sampling device is essential since it is through inadvertent and unknown contamination of the air that many laboratory infections occur. Furthermore, from the point of view of the Biological Laboratories' research program, valuable research information can be developed by the increased use of air sampling techniques by outside research institutions. Deterrents to the wider use of air samplers have been the lack of information about them and uncertainty about their availability and cost. A number of air sampling devices have been developed at the Biological Laboratories,[86] and a recent joint publication with the U.S. Public Health Service[87] trenchantly describes most microbiological air sampling devices to date.

During and after the study fellowship, I have been instrumental in making air sampling devices available to 13 U.S. laboratories on a loan basis. The air samplers were those originally designed by DuBuy and Crisp[88] and further developed by the Biological Laboratories. There is no commercial source for these sieve sampling devices, which are the cheapest and simplest

of the agar impingement samplers yet developed. A number of these samplers that had been declared surplus by the Biological Laboratories were turned over to the Technical Development Laboratories of the Communicable Disease Center, USPHS, for loan to qualified institutions. In addition to other air samplers which have been loaned by the Technical Development Laboratories, 50 samplers have been placed in research institutions as a result of personal discussions during the fellowship period. Directions for the calibration and use of the sieve samplers was also supplied.

E. PHOTOGRAPHY

I was allowed to photograph laboratory equipment and situations in 82 of the 102 laboratories. The result, a collection of almost 2000 color slides on 35 mm film, will be of continuous value in demonstrating various techniques, equipment, and design features used in the countries surveyed and constitute a permanent record of the fellowship activities. In addition, in a number of instances, the photographs provided me with a means of expressing my appreciation to laboratory directors for their cooperation and hospitality. Selected color pictures were mailed to these individuals in later correspondence. In 13 instances, laboratory directors requested that I send them copies of the pictures taken in their institute. None of the directors who allowed photographs objected to their use in published reports, but most requested that the laboratory not be specifically identified. Surprisingly however, seven directors invited the use of identified photographs from their laboratories as examples of improper equipment or technique.

F. SAFETY QUESTIONNAIRES

Laboratory directors and their employees were asked to fill out a questionnaire designed to explore the views of laboratory people on microbiological safety and accident prevention and, if possible, to point to any significant human elements that might be useful in reducing laboratory risks.

The questionnaire consisted of a single sheet, printed on both sides, containing 16 questions. Most questions could be answered by checking an appropriate short answer. Signatures and the identity of the laboratory was not requested. Completed questionnaires were separated only by country. General response to the questionnaire was poor. Only 202 were completed and returned from seven countries: U.S., 132; England, 17; Australia, 14; Canada, 12; Scotland, 11; Japan, 8; and Greece, 8.

Most participation was in English-speaking countries. A number of laboratory directors would not allow their people to fill out the questionnaires. Some of the reasons given for refusal were:

1. Irrelevant and personal information sought.
2. Doubted if information would be of any value to anyone.

3. Questionnaire not suitable for technicians.
4. Union permission required.
5. People already overburdened with reports and questionnaires.

Because of the small number of completed questionnaires, an analysis of the answers is of limited value. The results do, nonetheless, raise some general considerations about the attitudes and approaches of scientific personnel to laboratory safety. Compiled results from the 202 questionnaires are presented below:

GENERAL INFORMATION

Participants	M.D. degree	6.4%
	Ph.D. degree	13.4%
	Other degrees	49.0%
	No degree or No response	31.2%
Satisfaction with job assignment		
	Very much satisfied	55.9%
	Quite satisfied	38.6%
	Not much satisfied	4.0%
	No response	1.5%
Satisfaction with organization by which employed		
	Very much satisfied	43.6%
	Quite satisfied	48.0%
	Not much satisfied	6.4%
	No response	2.0%
Could you command a more important or responsible scientific assignment?		
	Yes	40.6%
	No	50.0%
	No response	7.4%
	Other response	2.0%
Are you satisfied with your relationships with fellow scientists?		
	Definitely	62.4%
	With some exception	35.6%
	No	1.0%
	No response	1.0%

MANAGEMENT ASPECTS OF LABORATORY SAFETY

Is your management sufficiently interested in the safety and welfare of the employees?		
	Yes	83.7%
	No	16.3%

Would greater scientific contributions result if there was less direction and regulation by management?

No doubt about it	8.4%
I think so	15.9%
Not necessarily	73.2%
Other response	2.5%

Do you have "human element" suggestions to improve the laboratory safety record?

Yes	22.3%
No	77.7%

SAFETY REGULATIONS

Should regulations be for non-professional help only?

Yes	7.9%
No	90.1%
No response	2.0%

Should each scientist be responsible for his own safety?

Yes	58.9%
No	39.6%
No response	1.5%

LABORATORY HAZARDS

Number of lost time or non-lost time accidents in last two years.

None	84.6%
One	11.4%
Two	3.0%
More than two	1.0%

Is much risk involved in the work you do?

Yes	38.6%
No	57.4%
No response	4.0%

Is risk-taking a normal or desirable part of everyday life?

Yes	53.0%
No	44.6%
No response	2.4%

Could you take greater precautions in your work?

Yes	69.8%
No	28.2%
No response	2.0%

Are work accidents and occupational illnesses practically unavoidable?

Yes	18.8%
No	81.2%

Anomalies in the above tabulation render conclusive statements impossible. For example, the fact that 57.4 per cent of the participants felt that there was not "much risk" involved in their work would suggest that many persons may not realize the seriousness of "ordinary" laboratory risks. Nonetheless, 69.8 per cent felt that they could take greater precautions in their work and 81.2 per cent felt that accidents and illnesses could be avoided. Surprisingly, 44.6 per cent felt that risk-taking was not a normal or desirable part of everyday life. The fact that 84.6 per cent of the participants stated that they had had no accidents in the last two years suggests that workers generally would not classify "minor irregularities" such as spilling cultures or dropping Petri plates as accidents. Over 90 per cent felt that safety regulations should apply to everyone and 73.2 per cent felt that direction and regulation by management were "not necessarily" preventing greater scientific contributions.

Space on the questionnaire was provided for additional written comments on the specific questions and for suggestions. A total of 119 comments were received, nine of which were irrelevant or related to the semantics of the questions. An analysis of the remainder of the comments is presented below under appropriate headings. Comments were from laboratory personnel in five countries; United States, Australia, England, Scotland, and Canada.

Frequency of Laboratory Accidents and Illnesses

Four participants indicated that they felt a distinction should be made between serious accidents and minor accidents, such as the breaking of laboratory glassware. One individual pointed out that it was difficult to prove the laboratory origin of illnesses among bacteriologists.

Feelings Toward Present Assignment and Employing Organization

One individual was "depressed by the germ surroundings" and was afraid of lung disease from automobile exhaust fumes. One person felt that he had too many irrelevant administrative duties, while another thought that his organization did a poor job with "public relations."

Are Work Accidents and Occupational Illnesses Practically Unavoidable?

One person pointed out that the breaking of laboratory glassware is practically unavoidable.

Effect of Management Directives and Regulations on Individual Accomplishments

Three individuals felt that present regulations and directives were not unduly restrictive. Two of the three indicated that they were subjected to only a minimum amount of administrative enforcement.

Should Each Scientist Be Responsible for His Own Safety?

There were 15 comments on this question. No one felt that a scientist should not be responsible for his own safety but a number of qualifications were entered. Four individuals were quick to point out that management also has a responsibility and two of these persons stated that the responsibility was that of enforcing adequate safety regulations. Two others, however, noted that few persons are sufficiently acquainted with laboratory risks to know how to write appropriate safety regulations. The thought that safety is a group responsibility was expressed by two individuals.

The importance of the acceptance of responsibility by scientists was illustrated by two participants. One noted that technicians will follow the work-habit examples set by the scientist and the other stated that the scientists who must train the technicians are often themselves inadequately trained in safety. Several other individuals were concerned about the responsibility for safety in fields or with equipment with which they were not acquainted.

Should Safety Regulations Be for Non-Professional People Only?

Two persons indicated that they felt that there should be separate safety regulations — "different levels of skill and background knowledge require different cautioning." One individual felt that safety codes, rather than regulations, should be used.

Can Greater Precautions Be Taken in Your Work? Is There Much Risk Involved?

Several individuals were concerned about the exact definition of the word "risk." Careful and precise techniques were considered important. Tiring of workers and the performance of routine jobs were mentioned as two factors leading to carelessness. Two persons stated that greater precautions were possible but not practical. Another indicated that the "means" must be provided in order to take greater precautions.

Could You at This Time Command a More Responsible Scientific Assignment?

There were various written comments made to this question, none indicated a definite no answer.

Is Risk-Taking a Normal or Desirable Part of Everyday Life?

Eighteen persons commented on this question. Five individuals objected to the form of the question. According to five others, risk-taking is a normal part of everyday life but is not desirable. Two persons qualified their answer with the statement that only the proper amount, or a calculated amount, of risk-taking is desirable. Other individuals made further qualifications, stating that the answer would depend upon the person, his age, marital status, etc. The difference between risks and "fool-hardiness" was mentioned by one participant. "Life is full of risks" according to two persons. One person stated that risk-taking is never desirable.

Suggestions, from a Behavioral Standpoint, for Improving Laboratory Safety

A total of 43 persons offered suggestions for improving safety in their laboratories. Six suggestions had to do with specific technical procedures which should or should not be done or the acquisition of new equipment. The remaining suggestions are summarized according to their relative frequency.

Eight persons suggested that greater emphasis be placed on training. Laboratory workers should be taught the correct techniques and precautions to be used.

Eight suggestions consisted of comments such as "think," "pay attention," "be careful," "act natural," and "avoid excessive talking."

Four persons thought that improved supervision would improve the safety record in their laboratory.

Four others felt that safety would be improved by reducing the volume of work or by avoiding rushing.

Three suggestions referred to the need for better laboratory safety regulations.

Two participants felt that overcrowding was responsible for hazards in their laboratories.

Two others stated that laboratory safety would be improved if personnel were reminded more frequently of the existing hazards.

Other comments were:

Stress importance of the responsibilities for safety.
Create better exchange of information.
Control emotions and be considerate.
Keep the risk value of old procedures fresh in your mind.
Avoid the accident-prone individual.

G. SALARIES OF FOREIGN SCIENTISTS AND LABORATORY WORKERS

During the fellowship year scientists and others at various laboratories mentioned salaries which were typical for that country. These figures have been summarized in Table XLIII along with the equivalent amount in U.S. dollars based on the exchange rate at that time. Unless one is able to equate this salary information to relative purchasing power, an accurate analysis is not possible. It is apparent, however, that the salaries in some countries are low when compared with American salaries.

TABLE XLIII. SALARIES OF FOREIGN SCIENTISTS AND LABORATORY WORKERS

COUNTRY	POSITION	SALARY PER MONTH	
		Local Currency	Equivalent Dollars
Australia	Department Head	350 Pounds	788
England	Technician	67-100 Pounds	188 - 280
Finland	Junior Technician	34,000 Marks	100
Germany	Professor Ordinar	1568-2320 DM	392 - 580
	Professor Extraordinar	1236-1664 DM	308 - 466
	Titular Professor	900-1500 DM	225 - 375
	Privatedozent	932-1500 DM	233 - 375
Germany (Hamburg)	Technician	400-500 DM	100 - 125
	Assistant (M.D.), starting	300-500 DM	75 - 125
	Assistant (M.D.), in 10 years	800-900 DM	200 - 225
Germany (Dusseldorf)	Institute Director	1400-1600 DM	350 - 400
Greece	Department Head	9000 Drachmae	300
	Staff Physician	4500 Drachmae	150
Netherlands	Industrial Director	1667-2500 Guilder	433 - 650
	Professor	1333 Guilder	347
	Lecturer, starting	833 Guilder	217
	Lecturer, after 5 years	100-1083 Guilder	260 - 282
	Lecturer, after 10 years	1250-1333 Guilder	325 - 347
	Chief Assistant (M.D.)	583-750 Guilder	152 - 195
	Assistant (M.D.), starting	417 Guilder	108
	Technician	250-583 Guilder	65 - 152
Portugal	Staff Physician	4000 Escudos	138
	Skilled Technician	2000 Escudos	69
	Junior Technician	1700 Escudos	58

H. TRAINING FILMS

Films made or sponsored by the U.S. Army Biological Laboratories were shown at various institutions in conjunction with the lectures (Table XLIV). These films have been made available to nongovernment institutions through loans from U.S. Public Health Service or through purchase from World Films, Inc. Two of the films (M-57 and FG-382) demonstrate the hazards involved in performing common laboratory manipulations and suggest corrective procedures. Two other films (M-261 and M-304) illustrate specialized equipment and techniques for research with infectious aerosols. Both sets of films, especially the first two, have created considerable interest in various areas of the world. During and after the fellowship period I received a number of requests and suggestions from U.S. and foreign laboratory directors who wished to use the films for training technicians. All of the directors with whom I studied have been supplied with purchasing information for the films.

TABLE XLIV. TRAINING FILMS USED DURING FELLOWSHIP

M-57	- "Infectious Hazards of Bacteriological Techniques," 16 mm film in sound and color, 13 minutes.
FG-382	- "Infectious Hazards of Bacteriological Techniques," 16 mm film in sound and color, 18 minutes.
M-261	- "Laboratory Methods for Air-Borne Infection, Part I, The Cloud Chamber," 16 mm film in sound and color, 30 minutes.
M-304	- "Laboratory Methods for Air-Borne Infection, Part II, The Henderson Apparatus," 16 mm film in sound and color, 30 minutes.

A frequent suggestion made by foreign scientists was that the U.S. Government make these films available for use through the offices of the United States Information Agency in the various countries. Several directors suggested that the films be supplied with the sound track in the language of that country.

Examples of the post-fellowship foreign use of these films are as follows:

1. Used in a training program for laboratory technicians by the Canadian Department of Health.
2. Used in a training program by the Australian Department of Health.
3. Through the World Health Organization, shown in schools for laboratory technicians in Afghanistan and Ceylon.

IX. CONCLUSIONS

A. OVER-ALL STATUS OF MICROBIOLOGICAL SAFETY

Research on infectious diseases can be carried on effectively only when adequate provision is made for the safety of personnel and for the security of experimental validity. Inadequate microbiological safety equipment and incorrect laboratory procedures will inevitably result in illness and loss of man hours and may result in fatalities among trained scientists or discontinuance of research projects.

The U.S. Army Chemical Corps Biological Laboratories is the world leader in microbiological laboratory safety. Although these laboratories and other selected institutions in this country and abroad have developed the basic concepts, techniques, and equipment needed, and although much of this information has been published, the majority of the infectious disease laboratories included in this survey were inadequately informed and equipped for safety. Only four of 102 laboratory institutions were considered to be completely adequate and sufficiently proficient in all aspects of microbiological safety.

This survey shows that there is need for critical experimental evaluation to determine

1. Under what conditions improvement in the safety of microbiological technique or equipment is desirable to reduce or eliminate human infectious hazards.

2. Under what conditions a change is unnecessary.

3. Under what conditions changes in technique or equipment are desirable to protect experimental or diagnostic validity, or the purity of the biological product.

4. Whether change in technique or equipment actually is effective. There is a strong tendency to institute a change based on best judgment, but to omit study of its efficacy. This is something like writing up the results of a proposed experiment without doing the experiment.

Although there is general recognition of current problems of microbiotic containment and laboratory infections, there appears to be a substantial lack of understanding and a consequent lack of application of safety technology. The most important difficulties are:

1. Failure to integrate safety objectives and policies into the laboratory program.
2. Lack of understanding of the mechanisms of aerosol formation by common laboratory manipulations.
3. Lack of understanding and acceptance of laboratory design principles, preventive techniques, and safety equipment.

Microbiological safety, as defined and discussed in this report, has several important ramifications when viewed on an international basis. The first relates to the immediate need and the present inability to carry out continuous laboratory operations with infectious materials during normal times without experiencing incapacitation of highly trained or valuable laboratory employees.

Second, the containment aspects of microbiological safety technology are important in their relationship to improving the reliability of medical research. The inability to achieve environmental control to a degree sufficient to prevent animal and culture cross-infection and other interfering phenomena is a detriment to the advancement of medical science. Furthermore, advances in the field of virology and the probability of the identification and isolation of the etiological agents of human cancer present increasing evident problems in laboratory environmental control and containment.

The third ramification is in the area of preparedness. In our present status of cold war and unrest, microbiological laboratories throughout the free world find themselves with an unsolved problem. In times of sudden and unsuspected need, such as in the case of disease epidemic or of overt biological warfare attack, are these laboratories sufficiently equipped, prepared, and trained to carry out their proper function?

Infectious operations are usually limited in size and scope, and the smallest possible amount of pathogenic material is handled. Whenever feasible laboratory workers are vaccinated. By trial and error over the years, laboratory personnel have developed techniques which are somewhat effective in limiting occupational illnesses. But for any laboratory suddenly called upon to function during an epidemic with a new or unidentified infectious agent, with an agent foreign to that part of the world, or with an existing agent with increased infectivity or pathogenicity, the above factors are of limited real value. In such an epidemic a large volume of laboratory work is likely to be required. Laboratory personnel may not be immune. An immunizing preparation may not be available; in fact, one of the tasks of the laboratory may be to attempt to devise a suitable vaccine. It is obvious that the laboratory would not be able to afford the time or the personnel to learn safe handling procedures by the trial and error method.

Although many laboratory directors are not prone to institute new measures to prevent laboratory-acquired infections and many prefer to believe that they have no microbiological safety problems, nearly all realize that laboratory manipulations with certain pathogens present unusual human hazards and agree that facilities capable of handling "high-risk" agents are needed in each country or in each area. They point to the large number of typhus infections that occurred during the war when many laboratories were called upon to produce typhus vaccine and to the laboratory epidemics resulting from the handling of Q fever organisms. They realize that in times of emergency (e.g.: epidemic or pandemic outbreaks of disease) almost any laboratory may be called upon to provide diagnostic service, to produce vaccines, and antisera, etc.

Some laboratory directors who relied on the immunity by active or subclinical infection as the best laboratory protective device stated that this system becomes unreliable when new or unknown disease agents are introduced into the laboratory.

Preparedness facilities of a type sufficient to provide absolute containment of highly infectious microorganisms exists at the present in only a limited number of microbiological laboratories. Those in Sweden were uniformly of a high standard.

The various chapters in this report illustrate the many worthwhile and significant contributions to microbiological safety which have been made at individual laboratory institutions. It is not the purpose of this overall evaluation to belittle these advances but, rather, to illustrate that only rarely are all of the components needed for continuous safe manipulations of infectious materials found in use at any one laboratory.

B. LABORATORY INFECTIONS

Sixty-five laboratories reported a total of 426 laboratory infections with 31 infectious agents and 17 fatalities. Twelve other laboratories had had infections but failed to give sufficient information for tabulation. Twenty-five laboratories reported no past infections. Tuberculosis, Q fever, brucellosis, psittacosis, and tularemia, in that order, were the most frequently occurring diseases. Together they comprised 78 per cent of the laboratory-acquired diseases. Noneducational, government, or state operated institutions used more types of infectious agents, had more persons at risk, and experienced more laboratory-acquired infections than did other types of laboratories.

In agreement with other surveys of laboratory infections, the exact cause of 86 per cent of the 426 cases was unknown, indicating the possible importance of the unsuspected release of pathogens by ordinary laboratory manipulations. Among those infections for which a cause had been determined, accidents resulting from self-inoculation, leaking aerosol chambers, cuts and bruises, centrifuge accidents, and sprays from syringes were the most frequent. Only two infections due to aspiration of infectious fluids were reported although oral pipetting was widespread.

It is concluded that laboratory-acquired infections are a problem in the majority of the laboratories included in this study.

C. MANAGEMENT ASPECTS

Sixty-nine per cent of the institutions were operated without an active and directed program for microbiological safety and 65 per cent failed to apply the basic accident and injury prevention principles generally used in nonlaboratory situations. Only 29 of 102 laboratories had written safety regulations. Twenty-one institutions had committees for laboratory safety

and 14 conducted training programs in microbiological safety and accident prevention. Ninety-three per cent of the laboratories administered vaccines to potentially exposed personnel.

From a management point of view there were three overriding deterrents to laboratory safety. One was the nonacceptance by laboratory personnel and directors of the safe way as being the correct way or as the way of good management performance. Another was the lack of interest among scientists in analyzing and discovering unknown causes and in developing new or alternate research methods with accident prevention and infection-free work in mind. The third was the low activity level among scientists in communicating to others information relative to corrective measures.

The most frequent shortcoming of laboratory management was the failure to program for safety. The failure was in not thinking of accident prevention in terms of a continuous necessity and in terms of a program which must be installed, planned, and implemented in the same way in which other activities are carried out. Furthermore, there was a failure to consider the human element in planning safety in infectious disease laboratories.

It is concluded that achieving safety in the infectious disease laboratory through the various management functions is not generally accepted in actual practice.

D. LABORATORY BUILDING DESIGN

Forty-three of 82 laboratory buildings were less than ten years old. About ten per cent were greater than 50 years old. Thirty new buildings were under construction or in the design stage and 15 buildings were less than one year old. Only 11 of the new or planned buildings incorporated adequate facilities for microbiological safety. The amount of space per person was sufficient in most laboratories.

In general, facilities for housing infected animals were more inadequate than those for laboratory operations.

Although many desirable design features of laboratories or animal houses are illustrated in this report, very few buildings contained all of the elements which would be considered necessary for infectious disease operations. In view of the activity in laboratory building construction and the large sums of money being invested in new facilities throughout the free world, it is tragic that so few modern designs show environmental control and containment. The principal problems are, (a) lack of detailed published information on design of infectious disease laboratories, and (b) inability to secure the additional funds required for laboratories of modern and adequate design.

Actually both problems involve communications since the procurement of funds often depends upon the availability of information on laboratory hazards and occupational illnesses to justify the higher costs of infectious disease facilities.

Modern laboratories equipped for infectious disease work may cost as much as $70.00 per square foot (Sweden). Buildings of adequate design were seen in the U.S., England, Sweden, Finland, and Denmark, but those existing or being constructed in Sweden more consistently exhibited adequate design criteria.

E. LABORATORY SAFETY EQUIPMENT AND APPARATUS

Although most infectious disease laboratories were reasonably well equipped with essential apparatus such as microscopes, balances, pH meters, and the like, there was a deficiency in the equipment and apparatus for decontamination, sterilization, and personnel protection.

Autoclaves, for example, were frequently poor in design, insufficient in number, and not properly located. Germicidal ultraviolet was widely used but without proper regard to testing and maintenance of the lamps. Available safety equipment for centrifuging, pipetting, blending, lyophilizing, or injecting animals was seldom used.

Although the Swedes, the British, the Canadians, and others have been active in designing ventilated microbiological cabinets, only 55 of 102 institutions used cabinets and of these less than ten institutions used cabinets of adequate design.

Sixteen laboratories held infected animals in some type of ventilated closure. In general, however, animal cages, cage racks, and equipment for animal autopsy provided little protection for workers in infectious animal quarters.

F. LABORATORY SAFETY PROCEDURES

The importance of safe procedures when handling infectious microorganisms was more generally recognized than was the need for special equipment and building design features. There was not, however, widespread understanding of the ease with which certain procedures can create air-borne contamination of the laboratory environment. Ironically, those procedures universally known to be of importance in preventing laboratory illnesses were only partially accepted. For example, the hazards of oral pipetting are well known yet 63 per cent of the institutions permitted this procedure. Only 30 per cent used needle-locking syringes although the hazards of injecting infectious fluids with friction-fitting needles are universally recognized.

Although procedures in a small proportion of the laboratories were governed by written regulation, there is need for general acceptance of adequately prepared procedural rules. Specifically needed is an adequate summation of research demonstrating hazards arising from various laboratory procedures. Also, in the development of new laboratory procedures there is a need to include aspects for personnel protection.

In general there was little evidence of adequate follow-up investigation to assess the value of those procedural changes made to improve safety. Methods of assessing microbiological hazards through the use of surface and air sampling techniques were infrequently used. Although many changes made on the basis of best judgment were probably effective in reducing infectious hazards, adequate validation of the effectiveness of these improvements would increase their general value, particularly when adopted in other laboratories.

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APPENDIX

APPENDIX

LABORATORIES VISITED AND LECTURES PRESENTED

AUSTRALIA

Canberra

Department of Microbiology, The John Curtin School of Medical Research, The Australian National University, Dr. Frank John Fenner, Head. Lecture presented - 27 April 1959.

Perth

Laboratory Section, Western Australia Public Health Laboratories, The Chest Hospital, Dr. William Laurie, Director. Lecture presented - 18 May 1959.

Melbourne

Department of Experimental Medicine, Walter and Eliza Hall Institute of Medical Research, The Royal Melbourne Hospital, University of Melbourne, Sir Mac Farlane Burnet, Director.

Commonwealth Serum Laboratories, 45 Poplar Street, Parkville, Dr. P. L. Bazeley, Director.

Department of Research, Fairfield Hospital, Fairfield, Dr. H. Mc Lorinan, Director.

Sydney

School of Biological Sciences, The University of New South Wales, Broadway, Dr. Bernhard J. Ralph, Head.

School of Public Health and Tropical Medicine, Commonwealth Health Department, University of Sydney, Prof. E. Ford, Director.

Adelaide

Department of Bacteriology, University of Adelaide, Dr. N. Atkinson, Head. Lecture presented - 4 May 1959.

Institute of Medical and Veterinary Science, University of Adelaide, Dr. J. O. Payton, Director.

AUSTRIA

Vienna

Institute of Hygiene, University of Vienna, Kenderspitalgasse 15, Dr. Von Hans Moritsch, Acting Director.
Lecture presented - 1 February 1960.

CANADA

Halifax

Department of Bacteriology, Dalhousie University and Nova Scotia Department of Public Health, Department of Laboratories, 62 University Avenue, Prof. C. E. van Rooyen, Director.
Lecture presented - 5 June 1959 - To Maritime Branch, Canadian Society of Microbiologists.

RCN Hospital Laboratory, HMCS "Stadocona," Lt. (M.T.) A. R. Westerbert, Chief.

Toronto

Division of Laboratories, Central Laboratory, Ontario Department of Health, 360 Christie Street, Dr. L. E. Elkerton, Director.
Lecture presented - 8 June 1959.

Spadina Division, Connaught Medical Research Laboratories, Dr. J. K. W. Ferguson, Director.

Hygiene Institute, University of Toronto, Dr. A. J. Rhodes, Director.

DENMARK

Copenhagen

Statens Seruminstitut, Amage Boulevard 80, Dr. Preben van Magnus, Director. Lecture presented - 20 November 1959.

ENGLAND

London

The Wellcome Research Laboratories, Langley Court, Beckenham, Kent, Col. H. W. Mulligan, Director, Biological Division.
Lecture presented - 14 July 1959.

Laboratory Animals Centre, Medical Research Council Laboratories, Woodmansterne Road, Holly Hill, Hampstead, Dr. W. Lane - Petter, Director.

The National Institute for Medical Research, The Ridgeway, Mill Hill, Dr. C. H. Andrews, Director.

Department of Bacteriology, Guy's Hospital Medical School, London Bridge, Prof. Robert Knox, Head.

Biological Department, Glaxo Laboratories Ltd., Greenford, Middlesex, Dr. J. Ungar, Director. Lecture presented - 17 July 1959.

Bacteriological Laboratory (M.R.C.), Public Health Laboratory Service, County Hall, Westminister Bridge, Dr. A. J. H. Tomlinson, Director.

Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, Praed Street, Mr. D. J. Flood, Chief Technician.

The Air Hygiene Unit and Streptococcal and Staphylococcus Reference Laboratories, Central Public Health Laboratories, Colindale, Dr. R. E. O. Williams, Director. Lecture presented - 20 July 1959.

The Lister Institute of Preventive Medicine, Chelsea Bridge Road, Prof. A. A. Miles, Director.

Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, Keppel Street, Prof. D. D. Reid.

Ross Institute of Tropical Hygiene, London School of Hygiene and Tropical Medicine, Keppel Street, Dr. George MacDonnald, Director.

Department of Bacteriology, London School of Hygiene and Tropical Medicine, Keppel Street, Prof. E. T. C. Spooner, Chairman. Lecture presented - 9 September 1959.

Liverpool

The Department of Bacteriology, School of Medicine, The University of Liverpool, Prof. A. W. Downie, Head. Lecture presented - 14 September 1959.

Sandwich

Biologicals Production Operations, Pfizer Ltd., Kent, Mr. J. C. Macsween, Chief. Lecture presented - 10 August 1959.

Macclesfield

Pharmaceuticals Division, Imperial Chemical Industries Limited, Alderley Park, Alderley Edge, Cheshire, Dr. D. Garnet Davey, Chief, Biological Group. Lecture presented - 31 August 1959.

Leeds

Department of Bacteriology, The School of Medicine, University of Leeds, Prof. C. L. Oakley, Chairman.

Porton

Microbiological Research Establishment, Ministry of War, Wilshire, Dr. David W. Henderson, Director. Lecture presented - 2 March 1960.

FINLAND

Helsinki

Institute of Serology and Bacteriology, University of Helsinki, Fabianenkatu 24, Prof. K. O. Renkonen, Head.

The Municipal Bacteriological Department, Aurora Hospital, Dr. Odd A. Wager, Director. Lecture presented - 11 November 1959.

The State Serum Institute, Prof. E. Uroma, Director. Lecture presented - 11 November 1959.

Microbiological Department, Orion Oy Pharmaceutical Co., Nilsiankatu 10-14, Dr. Timo Kosunen, Chief.

FRANCE

Paris

Virus Laboratory, Institute Pasteur, 25 Rue de Docteur Roux, Dr. P. Lepine, Director.

GERMANY

Berlin

Robert Koch Institute, Bundesgesundheitsamt, Nordufer 20, Prof. Georg Henneberg, Director. Lecture presented - 28 January 1960.

Bonn

Institute of Hygiene, University of Bonn, Prof. Gerh. Piekarski, Director, Medical Parasitology Department.
Lecture presented - 7 December 1959 - At American Embassy.

Dusseldorf

Institute of Hygiene and Microbiology, Medical Faculty, University of Dusseldorf, Witzelstrasse 109, Prof. W. Kikuth, Director.

Frankfurt

Paul Ehrlich Institute, State Institute for Experimental Therapy, Paul Ehrlich Strasse 42-44, Prof. Richard Prigge, Director.
Lecture presented - 22 December 1959.

Giessen

The Institute of Veterinary Hygiene, Justus Liebig University, Frankfurter Strasse 85-87, Prof. E. Roots, Director.
Lecture presented - 11 January 1960.

Hamburg

The Bernhard Nocht Institute for Naval and Tropical Diseases, Bernhard Nocht Strasse 74, Prof. Ernst Georg Nauck, Director.
Lecture presented - 18 January 1960.

Munich

The Institute for Infections and Tropical Medicine, University of Munich, Am Neudeck 1, Dr. Albert Herrlich, Director.

State Bacteriological and Public Health Institution, Lazarettstrasse 10, Dr. Blasius Freytag, Director.

Munster

Institute of Hygiene, University of Munster, Westring 10, Prof. H. Reploh, Director. Lecture presented - 14 January 1960.

Tubingen

The Institute of Hygiene, University of Tubingen, Silcherstrasse 7, Prof. Richard Ernst Bader, Director.
Lecture presented - 19 January 1960.

GREECE

Athens

Department of Microbiology, Faculty of Medicine, National University of Athens, 4 Dimocritou, Prof. Constantine Moutousses, Director. Lecture presented - 20 December 1960 - To Greek Medical Society and The Greek Society of Microbiology.

The Royal Hellenic Naval Hospital, Dinokriatous, Lt. George Papaevagelow, Head of Laboratory.

N.I.M.T.E. Hospital (Hospital for Retired Army Officers), Moni Petraki 10, Captain George Arabatzic, Head of Laboratory.

The Greek Seamens Chest Hospital, Melissia, Prof. Constantine Stephanopoulus, Director.

ITALY

Rome

Laboratories of Microbiology, Instituto Superiore di Sanita, via Regina Elena 299, Dr. G. Penso, Chief.
Lecture presented - 22 February 1960.

JAPAN

Nagoya

Department of Pathology, Medical School, University of Nagoya, Prof. Masasumi Miyakawa, Director. Lecture presented - 12 May 1959.

NETHERLANDS

Utrecht

The National Institute of Public Health, Sterrenbos 1, Dr. J. Spaander, Director-General.

Rijswijk

Medical Biological Laboratory, National Defense Research Council, RVO-TNO, Lange Kleiweg 139, Prof. J. C. Cohen, Director.
Lecture presented - 30 November 1959.

Leiden

Department of Medical Microbiology, Netherlands Institute of Preventive Medicine, Wassenaarseweg 56, Prof. J. D. Verlinde, Director.

NORWAY

Oslo

Institute of Hygiene, Norwegian Veterinary College, Ullevalsveien 72, Prof. Steinar Hauge, Director.
Lecture presented - 19 October 1959.

Institute of Bacteriology, University of Oslo, Ullevalsveien 33, Prof. S. Dick Henriksen, Director.
Lecture presented - 12 October 1959.

Institute of Hygiene, University of Oslo, Prof. Haakon Natvig, Director.

State Institute for Public Health, Geitmyrsvegen 75, Dr. Christian Lerche, Director.

Bergen

Department of Bacteriology, Gade's Institute, University of Bergen, Prof. Th. M. Vogelsang, Director.

State B. C. G. Laboratory, Overlegen, C. Sundsgate 57, Dr. Ivar Hesselberg, Director.

PORTUGAL

Lisbon

Instituto de Medicina Tropical, Prof. Manuel R. Pinto, Subdirector.

SCOTLAND

Dundee

Bacteriological Department, Queens College, University of St. Andrews, Prof. W. J. Tulloch, Director.

Aberdeen

Department of Bacteriology, University of Aberdeen, Foresterhill, Prof. Alexander MacDonald, Head. Lecture presented - 18 August 1959.

Glasgow

Science Bacteriology Department, Anderson College, 56 Dumbarton Road, Dr. R. B. Morrison, Head.

Bacteriology Department, Western Infirmary, University of Glasgow, Prof. J. W. Howie, Head.

Virus Reference Laboratory, Ruchill Infectious Disease Hospital, Dr. N. R. Grist, Chief.

SWEDEN

Stockholm

The Central Bacteriological Laboratory of Karolinska Hospital, Dr. Hans Ericsson, Director.

Swedish Research Institute of National Defense, FOA-1, Sundbyberg 4, Prof. Gustaf Ljunggren, Director. Lecture presented - 28 October 1959.

The Central Bacteriological Laboratory of Stockholm City, Dalagatan 11-B, Prof. Thorolf Packalen, Head.

The State Bacteriological Laboratory, Huvudsta, Solna, Prof. Gunnar Olin, Director.

Department of Virus Research, Karolinska Institute, Huvudsta, Solna, Prof. Sven Gard, Director.

The Department of Bacteriology, Karolinska Institute, Prof. B. Malmgren, Chairman.
Lecture presented - 26 October 1959 - To Swedish Society for Microbiology. Lecture presented - 3 November 1959.

Lund

Department of Bacteriology, University of Lund, Prof. Rune Grubb, Head. Lecture presented - 28 September 1959.

The Institute of Hygiene, University of Lund, Magle L., Krykog 9-A, Prof. Hans E. Ronge, Head.

Germ-Free Animal Laboratory, Department of Pathology, University of Lund, Prof. B. Gustafsson, Head.

Malmo

Department of Bacteriology, Medical School of University of Lund, Prof. Sten Winblad, Head.

Gothenburg

Bacteriological Institute, Medical School, University of Gothenburg, Prof. Orjan Ouchterlony, Head. Lecture presented - 2 October 1959.

B.C.G. Laboratory, The Municipal Bacteriological Laboratory, Dr. Olle Sievers, Head.

Tuberculosis Laboratory, The Municipal Bacteriological Laboratory, Dr. Orne Lind.

Sodertalje

Central Research Laboratory, Astra A/B, Dr. N. Ake Jonsson, Assoc. Director of Research. Lecture presented - 5 November 1959.

Uppsala

Institute of Bacteriology, University of Uppsala, Prof. Gunnar Laurell, Assistant Director.

SWITZERLAND

Bern

Swiss Serum and Vaccine Institute, Rehhagstrasse 79, Buenplitz, Dr. U. Krech, Chief, Virology Division.
Lecture presented - 8 January 1960.

Geneva

Health Laboratory Services Division, World Health Organization, Palais de Nations, Dr. R. Sansonnens, Chief Medical Officer.
Lecture presented - 4 January 1960.

UNITED STATES

New York, New York

The Rockefeller Institute, Dr. Frank L. Horsfall, Jr., Vice President.

New Orleans, Louisiana

Department of Infectious Disease, Tulane University Medical School, 1430 Tulane Avenue, Dr. Anees Mogabgab, Jr., Chief.

Los Angeles, California

Department of Infectious Disease, University of California at Los Angeles, Dr. Charles M. Carpenter, Chairman.
Lecture presented - 8 April 1959.

Department of Bacteriology, University of California at Los Angeles, Dr. M. J. Pickett, Chairman.

Clinical Laboratories, University of California Hospital, Dr. Frank Mc Kee, Director.

Pearl River, New York

Virus Research Laboratories, Lederle Laboratories, Dr. Harald R. Cox, Director. Lecture presented - 9 March 1959.

Chamblee, Georgia

Laboratory Branch, Communicable Disease Center, Mr. Earl H. Arnold, Assistant Chief.

San Francisco, California

The George William Hooper Foundation, University of California Medical Center, Dr. K. F. Meyer, Director.
Lecture presented - 6 April 1959.

Department of Animal Care, University of California Medical Center, Dr. Charles R. Riggs, Chief.

Medical Laboratories, Moffitt Hospital University of California Medical Center, Dr. W. L. Bostick, Director.

Carbondale, Illinois

Department of Microbiology, Southern Illinois University, Dr. Carl Lindegren, Chairman. 2 Lectures presented - 27 February 1959.

Branch Laboratory, Illinois State Health Department, Dr. Nathan Nagle, Chief.

Denver, Colorado

Department of Research and Laboratories, National Jewish Hospital at Denver, Dr. Gardner Middlebrook, Director.

Madison, Wisconsin

Department of Bacteriology, School of Agriculture, University of Wisconsin, Dr. Joe B. Wilson. Lecture presented - 26 March 1959.

Laboratories of Medical Microbiology, Department of Medicine, University of Wisconsin, Dr. Donald W. Smith.

Wisconsin State Laboratory of Hygiene, Dr. W. D. Stovall.

Durham, North Carolina

Microbiology Department, Bell Building, Duke University Hospital, Dr. Norman F. Conant, Chairman.

Department of Surgery, Duke University Hospital, Dr. Deryl Hart, Chairman.

Pittsburgh, Pennsylvania

Department of Epidemiology and Microbiology, Graduate School of Public Health, University of Pittsburgh, Dr. W. Mc D. Hammon, Chairman. Lecture presented - 24 March 1959.

Newark, New Jersey

The Laboratory, The Prudential Insurance Company of America, Dr. Raymond Jonnard, Assistant Director.

Philadelphia, Pennsylvania

Henry Phipps Institute, University of Pennsylvania, 7th and Lombard Streets, Dr. Julius Wilson, Director.

Kalamazoo, Michigan

The Upjohn Company, Mr. Bradley Reid, Assistant Manager. Lecture presented - 20 March 1959.